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The Edward Stirling Lectures.[1]

LECTURE II: DEMYELINATING DISEASE.

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IN the first G. E. Rennie Memorial Lecture delivered before The Royal Australasian College of Physicians on September 26, 1941, Weston Hurst (then of the Institute of Medical and Veterinary Science of this city) said: "It seems fitting therefore that in this first lecture . . . I should consider some of the unsolved problems confronting the neurologist; preeminent among these, and much under discussion at the moment, are the demyelinating diseases of man and animals." What a pity it is that I have to say the same thing tonight! It is an index of the difficulty and complexity of the problem that, despite the 19 years that have passed and the money that has been spent, it should be necessary to begin this lecture in the same way.

There is no doubt that demyelination of nervous tissue, and the diseases of which it is a characteristic, constitute the greatest enigma confronting neurological medicine today. Of course, there is scarcely a disease of the central nervous system that does not include demyelination in its pathology, but in the group generally considered under the heading of demyelinating diseases, the myelin sheaths are primarily involved, the axons and neurons in many instances being relatively unaffected.

I propose, then, to enumerate the various demyelinating disorders and the factors and agents which are known to be associated with demyelination. Though this would appear to be an ætiological classification, it is not meant to be.

1. Allergic (presumably):

(*a*) Acute disseminated encephalomyelitis — post-vaccinal, post-exanthematous, post-infective.

(*b*) Acute disseminated encephalomyelitis of uncertain ætiology, possibly following a non-specific infective illness.

(*c*) Acute hæmorrhagic leucoencephalopathy (Hurst).

(*d*) Acute disseminated demyelination associated with reticulo-endothelioses.

(*e*) Experimental encephalomyelitis (Rivers, Wolf-Kabat-Bezer).

2. Toxic:

Cyanide, lead, carbon monoxide, organic phosphorus compounds, sodium azide (Hurst), steapsin (Marburg, 1906), phospholipase, Marchiafava-Bignami disease.

3. Infective:

Virus (?)

[1] Delivered in Adelaide on May 10 and 12, 1960.

4. Nutritional:
   (*a*) Subacute combined degeneration.
   (*b*) Copper
   (*c*) Oxygen
   (*d*) Pantothenic Acid
5. Metabolic:
   (*a*) Porphyria
   (*b*) Lipodystrophies
   (*c*) Phenylpyruvic obligophrenia
   (*d*) ?Metachromatic leucoencephalopathy
6. Unknown:
   (*a*) Multiple sclerosis; neuromyelitis optica.
   (*b*) Diffuse cerebral sclerosis.

The variety of this list suggests that demyelination may be a common response of the central nervous system to varying noxious stimuli. Just as sarcoidosis is considered by some to be not a disease *sui generis* but a host reaction, so demyelinating disease may be a form of reaction to noxæ of various types. It is uncertain as yet whether the reaction, though resulting in demyelination, is the same in all cases. One would think that destruction would be the mode of action in the toxic group; but in that and in others demyelination may result from an interference with the formation of myelin. Rossiter, in speaking of his earlier research, said:

> We looked in demyelinating lesions and degenerating nerves for enzymes which would destroy myelin. We thought at the time this was the logical approach but although these enzymes can be found, they appear in a nerve quite late and we soon became convinced that demyelination is really due to a defect in the production of myelin rather than to an excessive breakdown.

Of course, it would be possible for a toxic substance to interfere with the mechanism of myelin formation, such as an enzyme system; but we have no clue as to the nature of the chemical mechanisms or of the enzyme system involved. There is evidence that myelin is in a constant state of rapid turnover, breakdown and reformation continuously taking place, and interference with this contant synthesis may result in the pathological process of demyelination. Why this process should occur in localized areas, or plaques, as in so many of the demyelinating diseases, is another of the mysteries of this type of nervous disorder.

Where so much is unknown, in a review of this kind I can but touch upon some of the features of these diseases which have interested me personally and hope that they may interest you also.

First, to consider the so-called allergic factor in the production of demyelinating disease. Let us take first the acute disseminated encephalomyelitis which follows vaccination or the exanthemata. By analogy with acute glomerulonephritis, in which the occurrence of some form of tissue hypersensitivity and antigen-antibody reaction is very suggestive, a similar mechanism would appear very probable here also. Let us consider the commonest disorder of this type—post-vaccinal encephalomyelitis. It occurs twenty times more frequently after primary vaccination than after revaccination. The interval between vaccination and the appearance of symptoms varies from 7 to 12 days, being mostly 10 to 12, a period which corresponds closely with the local and in some cases general eruption, and which may be considered to be a time when tissue reaction, both local and general, is at its height. The suggestion here of sensitization of nervous tissue and an allergic reaction is strong.

During a visit to New York in 1946-1947, I was able to see the work of Wolf, Kabat and Bezer, which seems to be allied to the phenomena described above. Rivers and his co-workers (Rivers and Schwentker, 1935) had already shown that demyelination could be produced in the rhesus monkey by many and repeated injections of a rabbit-brain suspension. By making a water-in-oil emulsion of brain tissue with paraffin oil, and adding aquaphor and heat-killed tubercle bacilli—Freund adjuvants, as they are called—which were known to enhance antibody formation to a variety of antigens, Kabat, Wolf and Bezer (1947) were able to produce encephalomyelitis in rhesus monkeys in a very short time, and with only one to three injections. It is interesting to note that this reaction could not be produced with emulsions of fœtal rabbit brain; nor could it be produced by adjuvants alone, or by adjuvants *plus* emulsions of other organs, or muscle, or skin. It followed the use of emulsions of spinal cord of rabbits three days old, or older, but did not appear after the use of cerebral tissue until the animals were 12 days old or older. These facts would suggest that the antigen involved in producing the disease, if not myelin itself, is at least formed simultaneously. Another point of interest in this work was that the tubercle bacilli had to be present with the brain tissue, or encephalomyelitis did not follow. The adjuvant action of these organisms seems to depend upon a somatic protein constituent of the bacillus. Moreover, in the nervous tissue the active agent also appears to be a protein or protein-bound, rather than a lipid. The complexity of the antigenic material used has led some to doubt the validity of this work in illuminating the problem of demyelinating disease. Nevertheless, the basic probability of an antigen-antibody reaction remains.

Another problem associated with acute disseminated encephalomyelitis, particularly the form of uncertain ætiology—(*b*) in our classification—is its relation to multiple sclerosis. Does this form, if different originally, ever become multiple sclerosis? Or does multiple sclerosis ever begin as acute disseminated encephalomyelitis?

This is the history of a patient whose illness I consider represents an example of acute disseminated encephalomyelitis of undetermined ætiology.

A man, aged 34 years, while on holidays at a beach developed paræsthesiæ in the right axilla, pain in the eyes and difficulty in lateral ocular movements. His temperature rose, and within two days he had headache, neck stiffness, pain and difficulty in moving the arms, sphincteric disturbance and a progression of paræsthesiæ from the arms down the trunk to the toes. Three days later frontal headache, pain in and stiffness of the neck and fever were still present. Paresis of eye muscles, arms and legs, bladder and bowel had developed.

On his admission to Sydney Hospital on February 12, 1954, he was quite clear mentally; the left pupil was larger than the right, but ocular movement was full without nystagmus. Neck rigidity was present. There was a quadraparesis, with no sensory loss, but increased deep reflexes, the plantar response on the left side was extensor. The cerebro-spinal fluid was clear and under increased pressure, and contained 70 cells per cubic millimetre, 90% of which were lymphocytes; its protein content was 50 milligrammes per 100 millilitres and its chloride content 630 milligrammes per 100 millilitres. The leucocytes numbered 13,500 per cubic millimetre of blood.

Over the next week his condition deteriorated and he became stuporose and irrational. His temperature rose daily to 102° F., paresis of the eye muscles developed and the other physical signs became more marked. Both plantar reflexes were now extensor, and sensation was lost below the tenth dorsal segment. Another lumbar puncture revealed a cell count of 120 lymphocytes per cubic millimetre, 50 milligrammes of protein per 100 millilitres, and 35 milligrammes of glucose per 100 millilitres. Liver function studies and a Paul-Bunnell test gave negative results. Virus studies were unobtainable. Tidal drainage was necessary. After a stormy illness lasting a month, this patient recovered. He is now very fit and plays 18 holes of golf, and the hesitancy of micturition and impotence which were troublesome for some time have cleared up. The deep reflexes are very active, but the plantar responses, which were extensor for some years, now are flexor. He is very well and leads an active business life.

These questions naturally arise: What was the ætiology—a virus infection, or post-infective encephalomyelitis of possible antigen-antibody reaction type? Was this an acute onset of multiple sclerosis? If not, will this patient develop multiple sclerosis?

In support of an allergic factor in the ætiology of post-infective encephalomyelitis, Van Bogaert has stressed the frequency of allergic skin and joint manifestations in both

the personal and the family histories of these patients. It is interesting to note that, at the age of thirty, this patient had a definite attack of gout.

German authors like Fraenkel and Jakob (1913) and later Pette (1929, 1938) have considered these cases to be "acute multiple sclerosis". Those of the "dualist" school, like Hallevorden and Spielmeyer, have insisted that acute encephalomyelitis of the type described and multiple sclerosis are entirely different diseases. I have allied myself with the dualists and have given it as my opinion that the patient will not develop that dread disorder.

Speaking in Adelaide, one should mention acute hæmorrhagic leucoencephalopathy, which was first described by Weston Hurst (1941) in this city. This is a fulminating illness which, again, seems to be preceded by a respiratory infection, often apparently insignificant, and the patient seems to make a complete recovery, only to be stricken in a few days by the rapid onset of all the symptoms and signs of a grave cerebro-spinal disturbance which ends in death, often in 48 hours. The acuity of the process is reflected in the cerebro-spinal fluid, which contains numbers of polymorphs and an increased amount of protein.

On section of the brain, the white matter is yellowish, and scattered hæmorrhages are numerous throughout its substance. In the cases in which brain-stem symptoms and signs have been predominant, similar changes are localized to the pons and medulla, although here the lesions are more symmetrical and involve both grey and white matter.

The characteristic histological change in this condition is necrosis of small blood vessels with the production of punctate hæmorrhages and extravasation of fibrin into adjacent neural tissue, necrosis of brain tissue and an intense cellular reaction, both locally in the region of the vessels and also in the Virchow-Robin spaces and meninges.

This type of disease is obscure in its origin and essential nature, but it is probably allied to acute disseminated encephalomyelitis, and its fulminating character may be related to a specific vulnerability of the host's tissue. Dorothy Russell considers these disorders to be variations of one pathological process with an allergic basis. She described three cases showing the gradation from one disease to the other, and in one, plasma cells in the spleen and a lesion of polyarteritis nodosa were present.

A similar factor may determine the differing pathological pictures seen in cases of "diffuse cerebral sclerosis". There has been considerable confusion in this group of demyelinating disorders, and various subgroups have been described on the basis of a family history, the age of onset and the rapidity of evolution and length of clinical course. They have been classified also according to their reactions to certain stains.

Schilder, whose name is always associated with this type of demyelination, really described three conditions (Schilder, 1912, 1913, 1924). His first report, in 1912, was of a condition with which we usually associate the eponym—namely, visual failure, mental deterioration and spastic paralysis. The patient was a girl, aged 14 years, who developed progressive right hemiplegia and died after an illness of six months' duration. The brain contained giant asymmetrical sharply demarcated plaques of demyelination and sclerosis occupying a large part of each hemisphere. It is noteworthy that there were also scattered demyelinating lesions throughout the brain and brain-stem. As Van Bogaert *et alii* have shown, there is no anatomical distinction between this type of condition and multiple sclerosis. Schilder's second report, in 1913, was of a case characterized by accumulation of a "prelipoid" substance. The condition seems to correspond more with a type of demyelinating disease to be described later as metachromatic leucoencephalopathy. The third case, reported eleven years later, was that of a woman, aged 37 years, who had suffered an attack of "influenza" one month before. Schilder recognized that the pathology of this case differed considerably from that of his former cases. It seems to correspond more with the subacute sclerosing types of leucoencephalitis which have been reported by Van Bogaert and others.

This group of demyelinating disease, diffuse cerebral sclerosis, includes a number of conditions which have been described under various names, but which are probably identical. The synonyms include encephalitis periaxialis diffusa, centrolobar sclerosis and Von Balo's concentric sclerosis, to mention but a few. They are all characterized by large and diffuse, often symmetrical, brownish-grey, semi-translucent lesions involving the central and convolutional white matter. It is remarkable how often the subcortical arcuate fibres are spared. The brain is involved in these cases much more frequently than the spinal cord.

In the majority of cases the disease appears to have begun in the occipital lobes, and an advancing margin indicates its forward spread into the parietal and frontal lobes. The corpus callosum may be involved, and spread may take place downwards into the internal capsule, brain-stem and pons.

The symptomatology, of course, depends upon the areas affected, and includes visual failure, mental disturbances, convulsive attacks, spastic weakness of limbs and sensory impairment of central type.

The metachromatic leucoencephalopathies were mentioned earlier. These have been called "Greenfield's disease" by eponymously minded Americans, both as a memorial and as a tribute to Greenfield's work in establishing these disorders as a definite clinical entity. In this group are included probably all of the conditions, some of which are familial, which show an abnormal accumulation of higher lipids. The oligodendroglia appears to be especially affected. In all sections of the white matter either these cells have disappeared, or their degenerate remains can be seen. The demyelination, too, is unusual and characteristic. It is diffuse and affects all the white matter, but particularly those tracts which mature late. This selective loss of myelin relative to the time of myelination is not seen in any of the other demyelinating diseases.

The lipid disturbance results in the aggregation of irregular spherical granular masses of lipid material. These are galactolipids, while phospholipids are scattered throughout the nervous tissue as fine granules. Cholesterol seems to disappear completely.

In a typical case the symptoms appear in the second or third year of life, and usually the illness ends fatally after a course of one or two years. The head may be large and suggest hydrocephalus. There is a disturbance in walking due to either spasticity or ataxia, more often unsteadiness, and at times nystagmus which would suggest a cerebellar lesion. These motor disturbances are followed by mental regression and sometimes convulsive attacks. Loss of vision appears relatively late in the course of the disease.

I believe that this disease is particularly important, because the metachromatic substances which have been found in the neuraxis are not limited to the central nervous system, but are found in the urine, in renal tubular epithelium, and in the Kupffer cells of the liver, and also in the gall-bladder, which they reach presumably through the blood-stream. Some cases were associated with chronic nephritis, for which, it has been suggested, these abnormal lipids may have been responsible. These granular masses may be stained both in the tissues and in the urine by a 0·02% solution of cresyl violet in acetic acid (1%). The wide distribution of these substances suggests that this disorder may be allied to the lipidoses, because demyelination may be found in Tay-Sachs disease, and the allied disease of Gaucher and Niemann-Pick. It is tempting to think, too, that a biochemical explanation for these maladies may be found, as it has been in disturbances like phenylpyruvic oligophrenia, Wilson's disease, Hartnup disease and so on, because the lipids in

these conditions are not abnormal, but it is the rate of their metabolism within affected cells which is impaired. This suggests the disturbance of an enzyme or enzymes concerned in the metabolism of these substrates for normal cellular function, and it may be postulated that the missing enzyme is a gene.

However, these disorders are rarities; but it is as well that we should know something of them, and that they should be mentioned in a review of this kind.

Multiple Sclerosis.

The demyelinating problem with which we all have to deal is the unfortunately relatively common condition, multiple sclerosis. The adjective "multiple" has superseded now the former term "disseminated" in standard nomenclature. With the disappearance of neurosyphilis from our neurological clinics, this disease has become one of the commonest organic disorders of the nervous system to be seen today. This subject of multiple sclerosis is so large in itself that I can do no more than touch upon various aspects of the disorder.

Although we know so much about its symptomatology and pathology, we are still in ignorance of its cause, and treatment remains empirical.

The theories of its causation have been many and varied. The following list is somewhat historical, but comprises the causes which have been suggested both in the past and at the present time.

Theories of Ætiology.

(i) "Dysplastic" glial development (Strümpel-Müller); (ii) circulating myelinolytic toxin (Marburg); (iii) spirochætal theory (Kuhn and Steiner, 1917; Steiner, 1952; Steiner, 1954); (iv) vascular theories—(*a*) venous thrombosis (Putnam), (*b*) vascular spasm; (v) allergy; (vi) biochemical theories; (vii) herpes simplex.

1. The Strümpel-Müller theory was based upon the concept of a neoplastic glial development, which compressed myelin sheaths and vessels with the production of demyelination by ischæmia. This theory was propounded in ignorance of the normal reactive powers of the glia and is of historical interest only.

2. The circulating myelinolytic toxin theory was formulated by Marburg in 1906, as a result of his use of injections of steapsin, and much later was brought forward again by Brickner in 1930. It postulated the presence of a lipolytic esterase in the serum of patients with multiple sclerosis. Subsequently experiments by a number of workers have failed to confirm the presence of such myelin-splitting ferments.

3. Spirochætes were first stated to be the cause by Kuhn and Steiner in 1917. They named the organism *Spirochæta argentinensis*. Steiner again in 1928 claimed to have seen spirochætes in dark-ground preparations of autopsy material. He also described argyrophilic rods, spires and loops which he held were products of spirochætal degeneration. More recently (1954), Steiner has named another spirochæte, *Sp. myelophthora*, as the cause of multiple sclerosis. His work has received practically no support.

4. Though there is no doubt that perivenous demyelination may occur in multiple sclerosis, Putnam's theory of microthrombotic venous occlusions and their treatment by anticoagulants has failed to stand the test of time and experience. The incrimination of vascular spasm, likewise, is still no more than a theory. However, there is another mechanism in which vessels may play a part, and that is by vasodilatation, which allows diffusion of antibodies to enter the extracellular fluids bathing the myelin sheaths. If an antigen existed in this situation, such as a proteolipid from altered myelin, then an allergic reaction could take place which would affect the myelin sheath predominantly.

5. The allergic theory has been discussed in dealing with encephalomyelitis and experimental encephalomyelitis.

6. Biochemical theories usually indict enzymes, but little is known about enzymes which would be active against all the lipids.

7. The herpes simplex theory has been put forward by Albert Sabin. It is based upon the idea that the virus of herpes simplex might attack the oligodendrocytes and cause a recurring demyelinative lesion whenever the resistance of the patient to this virus fell. Sabin has attempted to show by fluorescent techniques the presence of antibodies to herpes simplex virus in the nervous system. Like other theories, this latest one still lacks proof.

Symptoms.

The symptoms of multiple sclerosis are exceedingly protean and will depend upon the site of the lesions. These commonly affect certain structures, notably the optic nerves, the pyramidal tracts, the sensory fibres in the cord or the cerebellar pathways. Any or all of these systems may be involved at once, and so is produced one of the characteristic features of the symptomatology of the disease—notably, evidence of multiple lesions. Another well-known characteristic of the disease is the tendency of the symptoms to decrease, and so the course of the disorder is characterized by remissions and relapses, the periods of remission varying from a few weeks to years. Finally, there is also a tendency for the symptoms to affect the same structures, and for each exacerbation to follow the same pattern as was laid down in the original attack.

I do not intend to discuss neuromyelitis optica separately, as I consider it a clinical variant of multiple sclerosis and not a separate disease.

In a survey of 1848 patients reported by McAlpine, Compston and Lumsden (1955), the initial symptoms of multiple sclerosis were set out as follows:

Motor weakness in one or more limbs	770	(42%)
Retrobulbar neuritis	393	(21%)
Paræsthesiæ	328	(18%)
Diplopia	235	(13%)
Vertigo and vomiting	140	(7%)
Micturition disturbance	82	(4%)

I have reviewed some 100 cases of this disease which I have seen over the last few years in my own practice. I was moved to do this because of a question addressed to me in the last few weeks by a general practitioner.

He had referred to me a married woman, aged 48 years, who had been diagnosed by a psychiatrist as having "myasthenia gravis". She gave a history of being unable to walk any distance or to garden for any length of time without fatigue and weakness of her legs. She had had to give up golf three years before because of tiredness and what she described as "footdrop" after playing. She said that with each of her three pregnancies, the first 21 years before, she could not walk and had had to hold on to things. This she attributed to weakness associated with hyperemesis. On examination, she was an emotionally facile person. Though she was right-handed, her right grasp was weaker than her left. There was no sensory loss or incoordination of the upper limbs. The abdominal reflexes were absent. The legs were slightly spastic and weak, especially the right, with very increased reflexes, bilateral extensor plantar responses, but no sensory loss to any modality. Upon my giving the opinion that she was probably suffering from multiple sclerosis, her doctor asked: "What is the prognosis?"

This is the question which concerns us all, and which prompted me to look into my records of the last few years in order that my discussion of this subject should not be entirely "replete with thoughts of other men".

There were 69 women and 34 men, 67% and 33% respectively, figures which are somewhat comparable with those of McAlpine and Compston in Great Britain—64·2% and 35·8%. The youngest age of onset was 10 years in the female group and 15 years in the male. The disease is exceedingly rare in the first decade. McAlpine *et alii* record only one patient aged 10 years among the 1072 patients. The oldest age of onset among the women was 57 years and among the men 49 years. The woman whose

disorder had started with retrobulbar neuritis at the age of 10 years is still, at the age of 57, leading a life of modified activity as a farmer's wife on the north coast of New South Wales. One woman, now aged 56 years, whose disease had been of the brain-stem type with remissions and relapses over a period of 30 years, is still carrying on as a school-teacher, and apart from easy fatigability has very few symptoms, and apart from bilateral extensor plantar responses, no signs. These cases emphasize that we need not be too gloomy in our prognosis in this most unpredictable disease. One could have been forgiven for thinking that the woman whose symptoms were installed with retrobulbar neuritis at the age of 10 years would have a bad prognosis, but she is still on her feet and carrying on, despite spastic ataxia 47 years later. I have records of a patient, not included in this group, who had a complete remission for 30 years. Denny Brown quotes another who had the disease for 58 years with a remission of 36 years followed by a relapse and disability. He also quotes two examples of complete cessation of activity of the disease: one patient was a woman, aged 79 years and still living at the time of writing; the other was a man who died of heart failure at the age of 74 years; both of them had had undoubted attacks of multiple sclerosis between the ages of 20 and 24 years, which had left characteristic but not incapacitating sequelæ. Sir Charles Symonds (Cumings and Kremer, 1959) also reports two cases in which the disease had been arrested for periods of almost 40 years.

A further scrutiny of my few cases reveals an identical frequency of symptoms with that published by McAlpine, Compston and Lumsden in their monograph—namely, weakness of the legs (easily the commonest symptom) 31%, retrobulbar neuritis 24%, diplopia 13%, paræsthesiæ 20%, brain-stem symptoms 13%. Three of the 103 patients, all women, began their illnesses with frankly psychiatric symptoms.

One is frequently confronted with the problem of a patient, usually referred by an ophthalmologist, with impairment of vision in one eye and, perhaps, some blurring of the disc. The question naturally is asked: Is this multiple sclerosis? From the statistical point of view there can be only one answer, and that is that the commonest cause of unilateral retrobulbar neuritis is multiple sclerosis. As a corollary to the first question, one might pose a second: Are there any other causes of unilateral retrobulbar neuritis? With the disappearance of neurosyphilis from the clinical scene, the chances of an alternative pathological basis are still further reduced. In the presence of gross dental or paranasal infection, one would naturally treat the condition and hope; but as retrobulbar neuritis may occur as an isolated phenomenon in multiple sclerosis and may not be followed by other symptoms of the disease for years, if ever, it is very difficult to state dogmatically that the visual symptoms were the result of sepsis.

On one point it is possible to be optimistic: however severe the loss of vision, it is possible for a remarkable recovery of function to take place, and provided no further attacks occur, which is always a possibility, a central scotoma may remain the only sequel of the incident.

Nine of the 69 women noticed onset or exacerbation of symptoms either during pregnancy or immediately after parturition. I know that the number of patients I am quoting is far too small to make any ex-cathedra statement upon such an important and delicate subject. McAlpine, after a careful statistical analysis, states: "From these studies it can be concluded that the long-standing view of the relationship between pregnancy and the onset and course of the disease must be considerably modified." Nevertheless, this question arises with such frequency in my practice that I find it a real problem. Denny Brown (1952) states that though the relationship is haphazard and uncertain, "pregnancy is associated with relapse in 40% of women with multiple sclerosis". Of course, there are other factors than the pregnancy itself. There may be periods of enforced rest in bed; there is frequently administration of a general anæsthetic; both of these may be precipitants of symptoms. I have more than once in consultation seen symptoms of multiple sclerosis become manifest after a surgical operation, and I have felt that the stress of the anæsthetic and operation, *plus* the period of confinement in bed, has brought into the open symptoms and signs which may have been latent before.

Six of the 69 women are known to have died, one after a course of 19 years, from a fulminating bladder infection. One, after beginning with psychiatric symptoms, proceeded to a rapid termination after only three years. A third died after an illness of four years, presumably from an exacerbation of the disease, and a fourth after symptoms lasting 15 years. The cause of death in this case and in the fifth are not known. The sixth died a hopeless dement.

Two of the 39 men are known to have died, one after two years and the other after five years, both from acute exacerbation of the disease. The former, with marked involvement of the brain-stem, presented in one severe relapse the unusual combination of multiple sclerosis and delirium tremens. He went into a fairly good remission, but died soon afterwards from a rapid exacerbation of his malady.

In reviewing the records I have noted that four patients exhibited symptoms which I find particularly interesting—that is, the symptoms of sudden onset. One young man said: "Off and on my legs would be bad in a matter of moments." A young woman, on getting up after the birth of her first child, said: "My legs suddenly gave way, and after this they were heavy and I had a tight bandlike feeling round my waist." Another young woman, whose symptoms have been particularly apparent in association with two pregnancies, said: "I will suddenly be unable to move my legs and if standing will remain rooted to the spot. After a matter of about ten minutes I will be able to move, but my legs feel very heavy." Two features of the case of a third woman were these symptoms of sudden onset and a peculiar psychical disturbance which I have encountered in another patient, also a young woman. She described these symptoms as follows: "Suddenly my leg would go weak and I would be as if walking on air"; and "When most tense and even on the verge of tears I would be inclined to giggle although I would not feel giggly." Sudden exacerbation of symptoms is known to follow violent exercise, hot baths, excitement or emotion. Surely there must be a clue to the disease in symptoms of this type which are well known. Vision may become blurred or an eye practically or totally blind in a matter of seconds. What is this—an electrical or a chemical fault? There is nothing in the pathological findings to suggest that it may be vascular.

The Familial Element.

Finally to refer to the familial element in this disease. The familial prevalence is, in more than one series, stated to be 6·5%. One patient in my series had a sister with the disease, whom I saw. They stated that they thought their father must have had the disease, as he was paralysed, lived his last years in a wheel-chair and died at the age of 47 years. Though suggestive, this is by no means certain. The mother of one patient had the disease and the father of another died of it. One patient was interesting, in that her sister-in-law and the sister-in-law's sister both had the disease. These patients did not live together, so there was no question of an environmental factor.

Mention of environment brings up the tantalizing subject of what might be called in Hollywood parlance "The Swayback Story". I mention it briefly in case some of you may not have heard it, and in any case it should receive some notice in a review of multiple sclerosis. Let me be forgiven if I mention to this audience that swayback is a non-infectious, paralytic disorder of lambs born of ewes which have grazed on country the soil of which is deficient in copper. A massive symmetrical demyelination of the hemispheres is produced, which is remarkably like the pathological picture of some forms of diffuse cerebral

sclerosis that I have discussed. In 1947, Campbell *et alii* reported the occurrence of symptoms and signs of a disorder indistinguishable from those of multiple sclerosis in four of seven workers who had been engaged in research in this disease at Cambridge. The same writers later reported six cases of multiple sclerosis from a small village in Berkshire, five of the patients having attended the same school, and nine cases from another village in Gloucestershire. Sutherland, now of Brisbane, who made a survey of the incidence of this disease in the northern islands of Scotland (Sutherland, 1956), found three girls who were friends affected, three neighbours living in the same street and two game-keepers who had lived in the same house in succession. These facts make one think of a possible infection or some factor which allows an endogenous mechanism to operate.

Pathological Features.

The dominant pathological feature of multiple sclerosis is demyelination with relatively little destruction of axons. This was recognized originally by Charcot, and his descriptive name for the disease *"sclérose en plaques"* refers to two important characteristics of the lesions, sclerosis and a sharply defined affected area.

At autopsy superficial inspection of the brain, mid-brain and spinal cord may reveal nothing at all abnormal. In other cases the brain may appear somewhat atrophic, with an excess of fluid over the surface of the hemispheres and widening of the sulci. Plaques when present are more often seen on the ventral surface of the pons and in the spinal cord. They appear as greyish areas sharply defined and somewhat depressed below the general surface of the neuraxis. They are often unilateral and asymmetrical. Similar lesions may be found in the optic nerves, involving the whole of it or one side of it for a variable distance.

On examination of sections of the brain or neuraxis the greyish, demarcated, slightly gelatinous-looking areas are easily seen scattered throughout the nervous substance. Their number, size and shape vary greatly from case to case.

Histological preparations are best stained for myelin, when the sharply defined plaques may be seen as demyelinated areas. With higher magnification some myelin sheaths are seen to extend into the demyelinated areas for variable distances. "Shadow plaques" may be seen, in which the myelin sheaths have not completely disappeared but are thin and less deeply stained, as if the demyelinating process had not been acute enough to cause complete destruction. These are more common in the cord and on the edge of a more completely demyelinated area.

One of the characteristics of the pathology of multiple sclerosis, and one which may possibly help to explain the typical remission of symptoms in this disease, is that a tract may pass through a demyelinated area with very little evidence of secondary degeneration occurring in it below the plaque, or an optic nerve may be demyelinated for a centimetre or more, while further back near the chiasma it is intact. In very long-standing cases, however, evidence of ascending and descending secondary degeneration may appear.

Another feature of the histology, as has been stated, is the survival of axons in the plaques. Greenfield and King (1936) examined 125 cerebral plaques and found only 10% of axons destroyed; of the remainder half showed moderate and half little or no axonal loss. It is probable that the demyelinating process which denudes the axon for a variable distance also produces a reaction in the axon which interferes with its conduction for a period. Recovery of its conductivity may be responsible for remission of symptoms. Those axons which are affected show tuber-like swellings, beading or fraying within the confines of the plaque, afterwards resuming their normal calibre and staining.

In the early stages of its formation a plaque is usually pinkish in colour owing to dilated capillaries, and with the low power of the microscope it can usually be distinguished from the normal tissue around it by its greater cellularity. These cells are of microglial origin and are in the process of lipid phagocytosis. This area of increased cellularity corresponds exactly to the demyelinated zone and is as sharply defined, perhaps with a greater aggregation of cells at the margin of the zone. Sometimes these lesions are so cellular as to be mistaken for encephalomyelitis.

The changes in the myelin sheaths are essentially the same as Wallerian degeneration, but are much more rapid. The sheaths swell and break up into segments, and then into ovoid masses which become progressively smaller and irregularly dispersed granules; these in turn are taken up by macrophages which become distended and form typical foamy cells. These disappear into blood-vessels and Virchow-Robin spaces, leaving the area denuded of myelin.

In old plaques cellularity is conspicuously absent. Some astrocytic nuclei remain in the plaques, but in the white matter oligodendrocytes disappear almost completely.

Neurons in the grey matter show remarkably little change. Neuroglial fibres increase in density in plaques, and it was this feature of gliosis or sclerosis in the plaques which led Charcot to give the disease the name *"sclérose en plaques"*.

In contrast to post-infectious encephalomyelitis, the lesions of which are almost always perivascular, the plaques of multiple sclerosis have no definite relationship with blood vessels, but, where they are included, fibrotic thickening of their walls is a common finding.

The Cerebro-Spinal Fluid.

Reference must be made to the cerebro-spinal fluid. Lumbar puncture has little effect on the course of multiple sclerosis, and there is no reason to withhold the procedure in any case in which the diagnosis is difficult and there may be a suspicion of compression. It is interesting that the fluid may be normal in all respects, and no diagnostic characteristic of the disease in the fluid exists. However, with appropriate symptoms and signs, an increase of mononuclear cells, a raised protein content and a "positive" Lange curve, with a negative Wassermann reaction, are extremely suggestive and would be regarded as diagnostic by some. The colloidal gold reaction, which is most characteristic of the disease, is the "first zone" or "paretic" type of curve.

Though more florid cases are more likely to be associated with an increase in cells and a rise in protein content, this is by no means always the case. The increase in protein content may be exclusively in the globulin fraction.

In summary, there is an increase in cells, usually mononuclear, in one-quarter to one-third of cases, with a rise in protein content in approximately one-third and an abnormal colloidal gold curve in about half.

Yahr and Kabat (1957), of New York, have studied the gamma-globulin content of cerebro-spinal fluid and serum. They found that in multiple sclerosis the gamma-globulin level was often raised in the cerebro-spinal fluid but remained normal in the serum. The more acute and more widespread the disease, the more frequently was this abnormality present, and they concluded that it was an expression of the severity of the disease. They considered also that some of the gamma-globulin might be synthesized within the central nervous system. They studied the effect of the administration of large doses of prednisone on these gamma-globulin levels, and found that a fall of about 70% in gamma-globulin levels in the cerebro-spinal fluid could be detected 11 to 21 days before a drop in the serum gamma-globulin level, which was also only of the order of about 30%. On their continuing the study over a long period, the serum gamma-globulin level slowly returned to normal, whereas the cerebro-spinal fluid gamma-globulin level remained suppressed. This differential

behaviour, they conclude, indicates that the central nervous system has a mechanism whereby it can produce gammaglobulin, and that this mechanism is intimately related to the demyelinating process.

Admittedly we are groping in the dark and we have no idea of what these various studies mean or their significance in the problem of multiple sclerosis. However, it is a fair assumption that they point towards an allergic ætiology rather than to any other.

Prognosis.

What are the features of the disease which influence prognosis?

(i) Age: in general, the younger the age of onset, the worse the prognosis.

(ii) Severity of original attack: the more severe, the worse the prognosis.

(iii) Severity of relapses: again, the more severe, the worse the prognosis.

(iv) Frequency of relapses.

These omens of a bad prognosis are illustrated by the following case history.

A young woman aged 20 years, had complained of symptoms of 18 months' duration when I examined her. Her illness had begun with paræsthesiæ in hands and feet, which continued for four months. These disappeared, only to reappear and to be followed by weakness of the right leg and repeated falls. Then she had an attack of retrobulbar neuritis in one eye, which was quickly followed by rapid loss of vision in the other. She was practically blind when I saw her, and she died shortly after, her illness lasting only two and a half years.

The first five years will usually give an indication of the trend of the disease. The capacity to recover from a given attack improves with increasing duration of the illness, almost as if some immunity was developed.

Treatment.

Mention of the word treatment may perhaps raise a smile; yet I decline to admit to a complete therapeutic nihilism. Several admissions, however, have to be made at once: the bewildering variety of treatments that have been used without effect; the difficulty of assessing treatment in a disease subject to spontaneous remissions; and finally, the impossibility of applying rational treatment in a disease whose cause is unknown.

In the management of multiple sclerosis, treatment of the patient is paramount. Firstly, should one tell the patient the diagnosis? In the early stages, when often the nature of the malady may be no more than a suspicion, it would be wrong to communicate one's fears in case of error. When the diagnosis is certain, however, and evidence of multiple lesions is unequivocal, with support, perhaps, from examinations of the cerebro-spinal fluid such as I have mentioned, it is probably better to tell the patient the diagnosis in most cases, rather than resort to dubious euphemisms like "neuritis" or inflammation of the nerves. This is in the case of the apparently normal adult. For the younger and perhaps emotionally labile, probably female patient, other counsels may prevail and one's clinical sense may indicate that complete candour, at the moment, is unwise. The near relatives then could be informed of the *status quo*.

If the diagnosis is revealed, it should be followed at once by reassurance and emphasis upon the benign prognosis in many cases—that the wheel-chair is the rarity rather than the rule, and that every case is a law unto itself. The older the patient, as a rule, the milder the disease, the less the disability and the more prolonged the course.

With the onset of the disease, or with relapse, and symptoms affecting the lower limbs and locomotion, rest is essential. A comparison of multiple sclerosis with tuberculosis has been made, in that both diseases benefit from sanatorium treatment, which implies rest, warmth, accent on nutrition and vitamin therapy. Massage of weakened limbs would naturally be thought beneficial, but this is doubtful. When evidence of pyramidal tract involvement is present, it is better avoided as being likely to aggravate spasticity reflexly. After a preliminary period of complete rest, with signs diminishing and power returning, passive exercises of the limbs may be carried out, to be followed by assisted active exercises as progress continues. Of course, no form of electrical stimulation of the limbs should be considered.

The Alexanders and Berkeley, of Boston (Alexander, Berkeley and Alexander, 1958), in a carefully controlled study of long-term treatment, concluded that repeated blood transfusions, 500 ml. of whole blood or its equivalent in freshly spun-down plasma, once a week for six weeks produced a significant effect on the course of the disease. They also used ACTH, and considered it the treatment of choice in moderate to severe cases when attacks are fairly frequent with progression during intervals. They advocated a maintenance dose after the intensive treatment was over, and held that in this way relapses could be avoided or modified.

On the other hand, many reports of the use of cortisone or prednisone in the disease have been uniformly disappointing. Moreover, when improvement has occurred in cases in relapse, symptoms have recurred, often with greater severity, when the steroids were discontinued.

I have never used either of these methods, and mention them for what they are worth. In desperate cases either or both would be worth a trial, as the report was well controlled.

Mention has already been made of nutrition. This is important, and a high-calorie, high-vitamin diet with vitamin supplements should be given to maintain the patient's physical condition at an optimum. Any form of anæmia should be diagnosed and dealt with. Is vitamin B_{12} of any use? I must confess that in obstinate cases and with patients in relapse I use it. It at least does no harm and it may act as a metabolic stimulant with improvement in general health. Moreover, it has a good psychological effect, in that the patient is aware that an active form of treatment is being undertaken. Intravenous courses of "Novarsenobillon" may be in the same category, as there is no scientific evidence that either of these preparations has any specific effect on the disease.

Anæsthetics and operations, especially those involving prolonged immobilization in bed, should be considered only if they are absolutely necessary for improvement in general health or for saving life.

The problem of pregnancy has been considered before. It is probably wise to adopt the rule that pregnancy should be allowed only after two years of remission and when adequate post-natal care is available. When the patient presents with symptoms and signs of the disease and is pregnant, it is better to allow the pregnancy to proceed, as termination involves just as great a hazard of relapse and the psychological trauma may be greater.

In general, with a patient in remission, one should counsel the avoidance of over-fatigue, infections, chills and getting wet. Adequate rest and nutrition and vitamin supplements to maintain general health at its optimum should be stressed. The incidence of multiple sclerosis is greater in cold climates — for example, in Switzerland it rises to 7·4 per 10,000 in some areas. On the other hand, the disease is rare in certain warm climates, such as California, South Africa and Queensland. More than one writer has stressed the benefits of climate in the management of the disease, and the likelihood of remission being prolonged if a patient is in the fortunate position of being able to escape from the rigour of a very cold climate, where the risks of aggravating infections are also greater, to sunshine and warmth.

For those patients with considerable disability, particularly in walking, intensive physiotherapy such as is provided by clinics sponsored by the Multiple Sclerosis Society is of undoubted benefit, especially if the therapists

are of bright, vigorous and sanguine personality. There, too, the patients may learn a programme of exercises which they can continue after the intensive phase of the treatment is over.

Unfortunately, many tend to regress when removed from the optimism and encouragement of the clinic, which, besides physical treatment, provides a form of group therapy.

Conclusion.

I have placed these random thoughts on demyelinating disease before you because of its importance and its obscurity. It is only by constant review that we keep ourselves familiar with the innumerable facets of this group of elusive diseases. When more light is thrown upon this problem, what will the ætiology ultimately prove to be? I cannot do better than quote from C. E. Lumsden, Research Fellow of the Royal Society, who has laboured so long in this field (Lumsden, 1956):

> . . . here we have a biochemical mechanism capable of producing severe disease of the nervous system — of a microscopically visible inflammatory type — the process opens up a field of structural pathology as revolutionary as the discovery of the bacteria. If hypersensitization, or allergy, is in fact involved, then neuro-allergy becomes a scientific fact of the utmost respectability, and no longer a somewhat disreputable hypothesis concocted to cloak ignorance. — It is in this field that some of us are beginning to feel that we must search for the causative mechanism, not only of the post infectious myelinoclases, but of multiple sclerosis also.

To this I make bold to say, "Amen".

Ever since I stood in Elvin Kabat's laboratory, and saw the lesions he had produced in the nervous tissue of monkeys, and remembered the histological appearances that Oliver Latham and I had so often discussed, I have clung to the idea that somehow, in the long run, this view will prevail.

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NOTES ON INTUSSUSCEPTION IN A CHILDREN'S HOSPITAL.[1]

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IN any large centre where there is only one children's hospital, it is reasonable to suppose that the vast majority of children suffering from intussusception will be directed to this institution, and the available figures support this idea. In the 10-year period 1947-1957 there were recorded 422 cases at the Royal Alexandra Hospital for Children, and 64 cases at three other hospitals in this community which could be expected to take any significant numbers. These 64 cases were distributed as follows: The Royal North Shore Hospital, 21 cases; St. George Hospital, 12 cases; Renwick Hospital for Infants, 31 cases. This puts a responsibility on the staff of a children's hospital to place on record their results from time to time, to indicate trends in treatment and for comparison with other centres.

Our records (Table I) show that during this period the mortality rates of groups of consecutive cases approximating 100 have fallen from 7·5% in the first period to 0·9% in the last 112 cases.

The Irreducible Intussusception.

The major problem confronting the surgeon is the treatment of the irreducible intussusception. In the period under review, in 16 cases the intussusception was irreducible, in 11 it was treated by primary resection and anastomosis, and six patients died. Five patients were treated by exteriorization and three died. If these cases are taken in two groups, there were eight in the period 1946-1952, with only two recoveries and six deaths. One patient who recovered was a child of four years with a chronic intussusception and should properly be excluded from the discussion. If this is done, the results could not be much worse. Experiences like this produced widespread condemnation of resection and primary anastomosis (Strang, 1959; Jones, 1953), and alternative measures were adopted in many centres (Gross and Ware, 1948). Jones (1953) favoured a two-stage resection, and produced the remarkably good figure of eight recoveries in nine cases. In this procedure resection is carried out in the usual way and the abdominal wall is closed around the two adjacent limbs of the exteriorized loop. Bowel clamps are applied, the devitalized bowel is removed and a small Paul's tube is tied into each of the open bowel ends. This relieves the obstruction. The second stage, 48 hours later, consists in opening the abdomen again and anastomosing the two loops. If we consider the second group of eight cases covering the period 1952 to 1957, there were five recoveries and three deaths.

Of the five patients who recovered in the second period (Table II), four were treated by primary resection and anastomosis and one by exteriorization and ileo-transversostomy (White and Dennison, 1952). These figures show an improvement, and suggest that with modern methods of resuscitation primary resection and anastomosis should still have a place in treatment. In the fatal cases in this group the intussusception had been in evidence for periods of three, four and five days respectively. These late cases can be expected to carry a high mortality whatever treatment is adopted; but I think the best chance of survival will be in one of the less radical procedures not involving primary resection and anastomosis.

[1] Based on the Edward S. Stirling Lecture, delivered at Adelaide on August 27, 1959.

Primary resection is favoured by Swenson (1958) without qualification. As far as our own experience is concerned, I think in the past the fact that an intussusception was irreducible was not recognized early enough, and that futile attempts at reduction were persevered with when some other treatment should have been adopted earlier. This attitude of mind was brought about by the very bad results of resection and the determination to avoid it if at all possible. It is a matter of nice judgement to recognize the stage at which attempts at reduction should cease, and if this is done early I think resection with primary anastomosis is, in many cases, the operation of choice. In very late cases the safest procedure would appear to be ileo-colostomy, the mass being left in the abdomen, or exteriorization with resection outside the abdomen.

TABLE I.

Analysis of 422 Cases of Intussusception at the Royal Alexandra Hospital for Children.

Period.	Cases.	Deaths.
1946–1948	93	7 (7·5%)
1948–1951	111	5 (4·5%)
1951–1954	106	6 (5·6%)
1954–1957	112	1 (0·9%)
Total	422	19 (4·5%)

TABLE II.

Eight Cases of Irreducible Intussusception, 1946 to 1951.

Patient.	Year.	Duration of Intussusception.	Treatment.	Outcome.
A	1946	50 hours.	Resection of small bowel and end-to-end anastomosis; died in 4 days.	Death.
B	1946	36 hours.	Irreducible; exteriorization.	Recovery.
C	1947	30 hours.	Resection and end-to-end anastomosis; died in 48 hours.	Death.
D	1948	6 weeks.	Chronic intussusception. Resection and side-to-side anastomosis.	Recovery.
E	1949	2 days.	Ileo-transversostomy with exteriorization.	Death.
F	1950	48 hours.	Resection of small bowel and lateral anastomosis.	Death.
G	1951	2 days.	Resection of small bowel and side-to-side anastomosis.	Death.
H	1951	3 days.	Exteriorization and enterostomy; died one month later with encephalitis.	Death.
I	1952	4 days.	Resection of small bowel and side-to-side anastomosis.	Recovery.
J	1952	30 hours.	Resection of large bowel and end-to-end anastomosis.	Recovery.
K	1952	5 days.	Resection of small bowel and end-to-end anastomosis.	Death.
L	1953	4 days.	Exteriorization and ileostomy; died in 10 days.	Death.
M	1953	3 days.	Resection and end-to-end anastomosis.	Recovery.
N	1954	3 days.	Exteriorization and ileo-transversostomy.	Recovery.
O	1956	3 days.	Resection of large bowel and side-to-side anastomosis.	Death.
P	1957	36 hours.	Resection and end-to-end anastomosis.	Recovery.

Deaths after Reduction of Intussusception.

It must be remembered that not in all cases in which reduction is finally achieved will the patient recover. In this series there were 10 deaths in such cases. All these patients died in the first 27 hours, many of them a few hours after operation. Some might have been better treated by resection or exteriorization after an earlier assessment that the condition should be considered irreducible.

These figures again show improvement in the later part of the survey. In the case of Y the intussusception was satisfactorily reduced, but the child suffered cardiac arrest at the end of the operation. The heart was started again by cardiac massage, but the child died on the next day. The last patient never reached the surgeon's hands, but died in a medical ward. These two cases may be excluded from this particular discussion, so that since 1949 only two cases are left in which deaths occurred shortly after reduction of the intussusception. Perhaps better resuscitation has been the major factor in this improvement.

TABLE III.

Patient.	Year.	Duration of Intussusception.	Treatment.	Outcome.
Q	1946	30 hours.	Partial reduction with saline. Completed laparotomy. Death at 27 hours.	Death.
R	1948	3 days.	Shock. Excision of Meckel's diverticulum. Death at 24 hours.	Death.
S	1948	3 weeks.	Shock. Death at 10 hours.	Death.
T	1948	30 hours.	Reduction ileo-ileal. Death at 26 hours. ? Pneumonia.	Death.
U	1948	16 hours.	Reduction, caeco-colic. Death at 8 hours. ? Hepatic failure.	Death.
V	1949	3 days.	Shock. Death at 15 hours.	Death.
W	1952	34 hours.	Reduction and tears oversewn. Shock, 2 hours.	Death.
X	1952	36 hours.	Reduced easily. At autopsy, bowel satisfactory. Death at 8 hours.	Death.
Y	1953	12 hours.	Reduced, cardiac arrest. Death at 24 hours.	Death.
Z	1954	24 hours.	Shock. No operation.	Death.

Barium-Enema Reduction.

A feature of the procedure in treating intussusception in this hospital has been the increasing use of a barium enema as a preliminary to laparotomy, and this has now become almost a routine except in selected cases. For many years after Hipsley's (1926) notable work in this field, saline solution was used as the reducing medium; but in 1952 it was decided to follow the practice in other centres using conservative measures and test the use of a barium enema. This was found to have advantages, and has persisted as the method of choice. In 1952 a series of 39 patients were treated by this method, and in 28 the reduction was successful, only 11 needing operation. Figures taken from other years show considerable variation according to the enthusiasm of the surgical staff and radiologist; but the over-all figures show that in at least 61% of cases this procedure has eliminated the necessity for operation. These figures distinguish only between cases in which operation was performed and those in which it was not; operation to confirm reduction is counted as unsuccessful.

TABLE IV.

Results of Reduction by Barium Enema.

Year and Number of Cases.	Number of Successes.	Number of Operations.
1952: 39	28 (71·8%)	11
1956: 33	23 (69·4%)	10 (only 1 intussusception irreducible)
1957: 29	11 (37·9%)	18 (only 1 intussusception irreducible)
1958: 26	16 (61·5%)	10
Total (127)	78 (61%)	49 (38%)

It seems to me that the whole value of Hipsley's perseverance in the conservative method has been, not in reducing mortality at the time of operation (other factors have been responsible for this), but in preventing the handling of bowel necessitated by manual reduction and, as a corollary, in preventing intestinal obstruction as a late complication of laparotomy. In our experience there is nothing to support the view that reduction by barium enema is an added hazard which produces shock, especially if the procedure is reserved for suitable cases, is preceded by resuscitation and the setting up of an intravenous drip apparatus (Ravitch, 1958) and is carried out without anæsthesia. On the other hand, it is a common experience that intestinal obstruction due to bands or adhesions may occur even years after a laparotomy, and this may have been for the reduction of an intussusception or even the removal of a non-inflamed appendix. So far we have no record of this type of obstruction occurring after conservative reduction of an intussusception.

Chronic Intussusception.

To conclude these notes, I should like to mention two recent cases of chronic intussusception with rather unusual features. The only case occurring in this series has already been mentioned, and has been reported previously (Goulston, 1949).

Chronic intussusception is defined as intussusception in which the symptoms have persisted from five days to two weeks or more, and "there may even be diarrhœa" (White and Dennison, 1958). The usual concept is that the intussusception is loose, that obstruction to the lumen of the bowel is not complete and that the vascular supply is not interfered with. Hence the prognosis is usually more favourable than in acute intussusception.

CASE I.—A male infant was admitted to hospital at the age of 12 months with a history that his illness had begun three months before with pyrexia, vomiting and diarrhœa (with flecks of blood), when he was admitted to a country hospital. He improved under treatment but still had frequent yellow motions. He was admitted to the Royal Alexandra Hospital for Children with a diagnosis of marasmus (his wasted condition quite justified that term), and was treated for a further period of six weeks as suffering from cœliac syndrome. Quite by chance at one examination he was found to have an abdominal mass. A barium enema X-ray examination demonstrated that this was an intussusception, and this was reduced to the mid-colon quite easily. Laparotomy was then undertaken, and the intussusception was reduced to the ascending colon, but no further. In view of this child's precarious condition resection was not undertaken; but this seemed an ideal case for a simple short-circuit between ileum and transverse colon, the mass being left in the abdomen (White and Dennison, 1952). The baby recovered, and later X-ray studies show free passage of barium through the ascending colon, proving that the intussusception was reduced naturally after the swelling had subsided.

CASE II.—I am indebted to Dr. M. Sofer Schreiber for the details of this patient, to whom he was called in consultation, and on whom he successfully operated. A male infant, aged 11 months, was admitted to hospital with a two weeks' history of drowsiness, listlessness and vomiting after feeds. He had had diarrhœa for one week, with offensive stools, but without blood or mucus, and his abdomen was distended. He also was described on admission as "marasmic". The abdominal distension and diarrhœa continued, and he was thought to be suffering from colitis with toxæmia. X-ray studies four days after his admission showed dilated loops of bowel, but no fluid levels. Sigmoidoscopy was attempted, but was unsatisfactory owing to the volume of intestinal contents obscuring the field. Five days later his abdomen was still distended, and X-ray examination showed fluid levels. A barium-enema X-ray examination disclosed an intussusception in the transverse colon. At laparotomy this was reduced to the ascending colon, and ileo-transversostomy was performed with a good result.

The unusual features in these two cases are the extreme chronicity, the presence of chronic diarrhœa and the complete absence of anything suggestive of an intussusception in the early stages.

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SALK VACCINATION: REACTIONS AND SEQUELÆ. OBSERVATIONS IN WESTERN AUSTRALIA.

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SALK VACCINE has proved to be one of the most trouble-free immunizing agents ever used. Nevertheless, injection of this antigen has on rare occasions been followed by clinical phenomena of various kinds. Most of these incidents have been relatively minor, but several have been quite disturbing. The impending release of Salk vaccine for private immunizations involves an extension of its use by a much wider range of medical practitioners than hitherto. Some of these may be unfamiliar with the vaccine and may appreciate any information which will be of assistance in assessing such so-called reactions or sequelæ as are encountered. The following observations, which have been recorded in Western Australia during the course of the last four years, could therefore be of interest to private practitioners. During this period (July, 1956, to June, 1960) over 1,300,000 separate doses of Salk vaccine were administered to about 480,000 people (approximately 80% having received the full course of three injections).

The untoward incidents noted in Western Australia have, for convenience, been classified into six groups, although there is some overlap between these groups.

Dermatological Phenomena.

Transient Rashes.

A number of children have developed transitory rashes within 48 hours of injection. These rashes have not conformed precisely with the common childhood exanthems, but have perhaps simulated rubella more often than any other condition. These rashes have not recurred with succeeding injections and have seldom been accompanied by itching. Their significance is extremely difficult to evaluate. The association with Salk vaccine in many cases could have been coincidental; and it may be relevant that these rashes were most commonly reported during the early phase of the Salk vaccination campaign. If they are attributable to the vaccine, the basic mechanism is uncertain; but in any event, because of their transient nature, the absence of constitutional manifestations and their failure to recur with subsequent injections, these rashes are of little consequence and need occasion no undue concern to practitioners presented with them.

Urticaria.

A male infant, aged eight months, developed urticaria three days after his first Salk vaccine injection. Despite antihistamine therapy, weals recurred off and on throughout an entire week, and then disappeared. When he was

presented for his second Salk vaccine injection about a month later, an intracutaneous test dose of 0·1 ml. (one-fifth of the regular dose) was administered. An hour later there was no visible evidence of hypersensitivity, and nothing abnormal could be detected the following day. The normal second dose was therefore given, and the child again developed urticaria about four days after his injection.

A man, aged 50 years, had received two injections of Salk vaccine without incident. Eight months afterwards he obtained his third inoculation. Ten minutes later he vomited at his cafe and experienced generalized pruritus. He was brought back to the clinic with generalized urticaria accompanied by œdema of the eyelids. Adrenaline relieved his condition in a very short time. He had never had penicillin therapy, nor did he admit to any allergic episodes in the past.

Dermatitis.

Two examples of severe generalized dermatitis associated with Salk vaccination have been seen. Both patients were women.

The first case was that of a pregnant woman, aged 43 years, who developed "hives" a week after her first injection. She was treated with various antihistamines, but multiform cutaneous lesions appeared and persisted. She was regarded as suffering from allergic dermatitis, and was treated in hospital over a period of several weeks with cortisone, and eventually recovered.

The second woman, aged 45 years, had previously been treated for allergic dermatitis, but was more or less free from skin lesions at the time of her first injection of Salk vaccine. Twenty-four hours later, swelling and tenderness were present at the site of the injection, and there was an eczematous rash in front of the elbow. This apparently faded somewhat, and she returned for a second injection four weeks later. Twenty-four hours afterwards she developed urticaria of the face and neck, and the eczematous patch in the left ante-cubital fossa recurred. She was troubled off and on for the next 12 months with eczematous patches, mainly on the arms, head and neck, and was regarded as suffering from allergic dermatitis which had become aggravated by Salk vaccination. A skin test with highly diluted monkey kidney-cell protein was followed by a marked local reaction and an exacerbation of her dermatitis.

Antibiotic Sensitivity.

Penicillin.

During the preparation of Salk vaccine, penicillin is added to it in amounts not exceeding 100 units per millilitre, but it is stated that "the final vaccine has little or no penicillin activity". Evidence of penicillin reactions in persons injected with Salk vaccine has been looked for specifically.

A woman, aged 32 years, who had received penicillin injections some years previously, received her first Salk vaccine inoculation without incident. A month later she was given her second injection. Within five minutes she experienced intolerable pruritus and quickly developed multiple urticarial weals. She was injected with seven minims of adrenaline and experienced rapid relief. An hour later the itching had ceased and the weals had almost subsided.

A woman, aged 43 years, received two uneventful injections of Salk vaccine a month apart. Some time later she suffered from several incidental illnesses which were treated with penicillin given parenterally, and was said to have acquired hypersensitivity to this agent. When she presented for her third Salk vaccine inoculation, therefore, a test dose of 0·05 ml. (one-tenth of the regular dose) was injected intradermally into the skin of the right forearm. Ten minutes later there was a weal three inches in diameter at the site of the injection, and she complained of feeling sick. Her eyelids became swollen and there was marked lachrymation. She was relieved with 0·5 ml. of injected adrenaline-in-oil accompanied by an antihistamine preparation given orally.

Streptomycin.

One hour after her first injection of Salk vaccine, a nurse complained of irritation of the eyes, giddiness and nausea. Her face became flushed, her eyelids began to swell, and nasal obstruction developed. Within a short time her entire face was œdematous, and she presented the appearance of angioneurotic œdema. She was treated with antihistamines, improved rapidly, and had quite recovered four days later. At the time of the injection, it was not known that this nurse had been shown to be sensitive to streptomycin some months previously. She was unable to given an injection of streptomycin (even when wearing rubber gloves) without developing signs identical with those which had followed Salk vaccination.

The usual dose of Salk vaccine (0·5 ml.) contains about 50 μg. of dihydrostreptomycin (which is incorporated in the vaccine in order to safeguard against bacterial contamination), and it is especially interesting that such a small quantity is capable of provoking a florid reaction in a sensitive person.

Shoulder Joint Disorders.

A woman experienced pain "in her arm" shortly after her first inoculation. Two months later she received her second injection in the right triceps. Immediately afterwards she complained of pain at the injection site. The pain radiated to the elbow and to the finger tips, and was accompanied by numbness and tingling. This subsided, but on successive nights following this incident she was awakened by pain. Eventually the pain became localized to the region of the humero-radial joint, and three months later the joint was injected with hydrocortisone by her usual doctor. On examination some weeks later the joint was still tender, but the patient's symptoms were much less pronounced.

A nursing sister became conscious of an ache in the left arm a few days after her first injection of Salk vaccine. Discomfort involved the shoulder above and the forearm below. It interfered with her sleep. When she was examined about five weeks later, there was marked tenderness in the region of the supraspinatus muscle and shoulder joint. She was unable to raise the arm fully. Her hand grip was relatively weak, and sensation was undiminished. She was given analgesics, but there is no record of further examinations.

A railwayman was given his third injection of Salk vaccine. Two days later he experienced pain in the shoulder and was unable to put on his coat unaided. The pain persisted and disturbed his sleep. On examination of the patient a week later, there were no notable physical signs other than tenderness on palpation in the vicinity of the shoulder joint and some limitation of abduction. There is no further record of his progress.

A female school-teacher, aged 52 years, complained of pain at the site of puncture in the left arm immediately after her third Salk vaccine injection. The pain persisted, and about two months later she reported for examination and was referred to a specialist orthopædic surgeon, who diagnosed her condition as "a capsulitis of the shoulder joint — of the type not infrequently seen in association with injections in the upper arm". Movements at the joint were limited, especially abduction, and the joint itself was tender on direct pressure. She was treated with "Butazolidin" and made a slow recovery over the course of the next six months.

Neurological Sequelæ.

Three incidents have been encountered of muscle weakness and wasting attributable to nerve lesions. All three patients were in their fifties.

The first, a woman, aged 50 years, began to notice "pins and needles" accompanied by "cramps" of the little, ring and middle fingers of the right hand six weeks after her second Salk vacine injection. Weakness of the hand developed, together with reduced sensibility along the inner side of the hand. Two years after the incident, she has slight residual signs consistent with a mild ulnar palsy.

The second patient, a man, aged 57 years, noticed weakness developing in his left arm and shoulder about three weeks after his second inoculation with Salk vaccine. Specialist examination some two months later revealed muscle weakness corresponding with the distribution of nerve fibres from the fifth and sixth cervical segments.

The third patient, a man, aged 54 years, experienced an aching sensation along the inner forearm about two hours after his second injection. This ache persisted, and about six weeks later, when he was examined by a neurologist, he was found to have motor signs of a partial ulnar nerve lesion.

The first and third patients appear to have suffered from ulnar neuritis, while the second could have had radiculitis or brachial plexitis. In all three cases the basic mechanism was almost certainly not traumatic. Similar neurological sequelæ have been reported as following many other prophylactic agents (especially tetanus antitoxin). The mechanism is obscure and a selective hypersensitivity has been postulated.

Asthma.

A girl, aged 19 years, gave a history of having suffered from numerous attacks of asthma until the age of seven, when the attacks ceased. At 14 she became subject to frequent bouts of hay fever, and these still bothered her. She was given her first injection of Salk vaccine, and while on her way home some 10 minutes later she began to cough and experienced difficulty in breathing. She returned to the clinic, and was found on examination to have expiratory dyspnœa and bronchi indicative of an asthmatic episode. She obtained rapid relief from injected adrenaline and did not report any recurrence. Some weeks later a second Salk vaccine injection was administered without untoward effect.

Anaphylactoid Reaction.

A girl, aged six years, collapsed and nearly died three or four minutes after her second injection of Salk vaccine. She was on her way home in a car with her parents when she complained of a tightness in her throat, vomited and lapsed into unconsciousness. When medically examined a few minutes later, she was deeply cyanosed, her breathing was almost imperceptible and her pulse was impalpable. Her airway was cleared and artificial respiration applied, and she was removed to hospital and given oxygen *en route*. She recovered in about 20 minutes, but was detained in hospital overnight. She was reexamined about ten days later, but showed no evidence of illness. This child had suffered from recurrent episodes of eczema since infancy.

Commentary.

It is evident from the experiences described above that undesirable reactions from Salk vaccine injections can be expected; but it is also clear that in relation to the vast number of vaccinations performed without ill effect, the occurrence of these reactions will be extremely rare. Only one of the incidents described was really alarming (the anaphylactoid reaction). The shoulder-joint disorders and the neurological sequelæ were especially disturbing because of the prolonged discomfort and inconvenience involved. Unfortunately, these conditions are neither predictable nor preventible.

So far as antibiotic sensitivity is concerned, it is doubtful whether anyone who is known to be sensitive to streptomycin should ever be injected with this type of vaccine; but it is likely that some penicillin-sensitive people may be able to receive it without harm, if the result of a minute skin-test dose is satisfactory. Recurrent dermatitis could well be a contraindication, but further experience of these cases will be necessary before a firm opinion is reached.

In conclusion, therefore, it can be stated that although Salk vaccine has not proved to be absolutely free from undesirable reactions, these have been so few and far between that the vaccine may be generally regarded as one of the most acceptable agents ever used in the prevention of disease.

HÆMOPERITONEUM OF UNUSUAL ÆTIOLOGY.

By A. RUMORE, M.B., B.S.,

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THE outpouring of large quantities of blood into the peritoneal cavity sufficient to cause severe and often alarming symptoms is commonly due to gynæcological abnormalities or to trauma.

In a review of 129 consecutive cases occurring in the Oxford group of hospitals over six years (1952-1956), Ellis, Griffiths and MacIntyre found that in 68% the bleeding was of gynæcological origin (ruptured ectopic pregnancies or ruptured follicular cysts), and in 23% followed trauma to spleen, liver or both of these organs. There were four ruptured aortic aneurysms and two severe post-operative hæmorrhages. These authors encountered six examples of unusual origin which they described and discussed in detail. Table I shows the final diagnosis and mortality in the 129 cases they collected.

TABLE I.

Final Diagnosis and Mortality in 129 Consecutive Cases of Hæmoperitoneum. (Ellis, Griffiths and MacIntyre, 1958.)

Final Diagnosis.	Patients.	Deaths.
Gynæcological[1]:		
Ruptured ectopic pregnancies	77	0
Ruptured follicular cysts	10	1
Traumatic:		
Ruptured spleen	2	4
Ruptured liver	6	2
Ruptured liver and spleen	2	2
Ruptured liver and middle colic artery	1	1
Other causes:		
Intraperitoneal rupture of aortic aneurysm	4	4
Following operation	2	1
Unexplained at laparotomy	2	1
Ruptured primary tumour of liver	1	1
Rupture of stomach in hæmatemesis	1	1
Bleeding retroperitoneal varices	1	1
Hæmorrhage from juxtapancreatic vessel in hypertensive patient	1	1
Total	129	20 (16%)

[1] These cases exclude 36 unruptured ectopic pregnancies or clotted pelvic hæmatoceles and 15 ruptured follicular cysts with little or no bleeding.

Some of the other unusual causes of hæmoperitoneum found in the literature are as follows: (i) trauma to other abdominal organs (other than spleen, liver or blood vessels within the abdomen); (ii) dissecting aneurysm of the aorta; (iii) aneurysm of the splenic artery; (iv) aneurysm of the hepatic artery; (v) aneurysm on other arteries (for example, ileo-colic, mesenteric, left or right gastric, vessel in greater omentum); (vi) hæmorrhage from carcinoma of the liver; (vii) perforated carcinoma or ulcer of the stomach; (viii) hæmorrhagic diseases; (ix) hæmorrhage from a vein on a subperitoneal fibroid tumour; (x) hæmorrhage into the peritoneal cavity from retroperitoneal hæmorrhage.

Some cases are reported as "abdominal apoplexy", and a large number of cases are reported as spontaneous intraperitoneal hæmorrhage when no cause for the bleeding can be found either at laparotomy or at autopsy.

The occurrence of three rare examples of this condition within a short period of time (four months), and the fact that no reference to this condition can be found in many of the standard textbooks of surgery, have stimulated this paper.

Aird (1957) seems to include hæmorrhagic effusions, such as those produced in acute pancreatitis, mesenteric embolism and thrombosis, internal strangulations and torsion of the omentum, under the general heading of hæmoperitoneum. The three cases reported in this publication are unusual examples of hæmoperitoneum; but they do present important problems in diagnosis and treatment of the rarer and often fatal forms of massive hæmoperitoneum.

REPORTS OF CASES.

CASE I.—A male patient, aged 48 years, a storeman, was admitted to the Canterbury District Memorial Hospital with a history of having struck his face on a wardrobe 24 hours previously. He had not lost consciousness. Eight hours prior to his admission he had developed severe lower abdominal pain, which was continuous in nature

and increasing in severity. He was so preoccupied with his moderate facial contusions that he had not noticed a huge bilateral scrotal hæmatoma until just before his arrival in hospital. The patient had not vomited and had not passed urine, and his bowels had not opened since the accident. He had been aware of the presence of a left inguinal hernia for three years.

On examination, the patient was apprehensive and in obvious distress. He had moderate facial contusions. The temperature was 99° F., the pulse was regular at 100 per minute and the blood pressure was 130/80 mm. of mercury. There was marked tenderness of the lower part of the abdomen with generalized guarding. Bowel sounds were absent. There was a large amount of fæces in the rectum, and the prostate was not enlarged. The scrotum was grossly and evenly enlarged, the hæmatoma extending on to the lower abdominal wall, its upper margin being well demarcated by a greenish-blue line. Both inguinal regions were swollen and very tender. No hernia could be discerned on either side. Catheterization of the patient's bladder produced 22 oz. of clear urine. The hæmoglobin value was 15·6 grammes per 100 ml.

A diagnosis of scrotal hæmatoma, incarcerated left inguinal hernia and/or intraabdominal injury was made.

At operation, through a left inguinal incision extending into the upper part of the scrotum, a large persistent processus vaginalis was found distended with fluid blood and blood clot. The blood could be made to run readily up into the peritoneal cavity or down into the sac of the tunica vaginalis. When the hernial sac was opened, large blood clots and about one pint of blood were drained from the peritoneal cavity. Two small lacerations on the body of the testis were still bleeding actively. The hæmatocele was emptied, hæmostasis was obtained and the sac of the tunica vaginalis was excised and drained. The hernial sac was removed and the defect in the inguinal canal repaired. A blood transfusion was given, and the patient made an uninterrupted recovery. (See Figure I.)

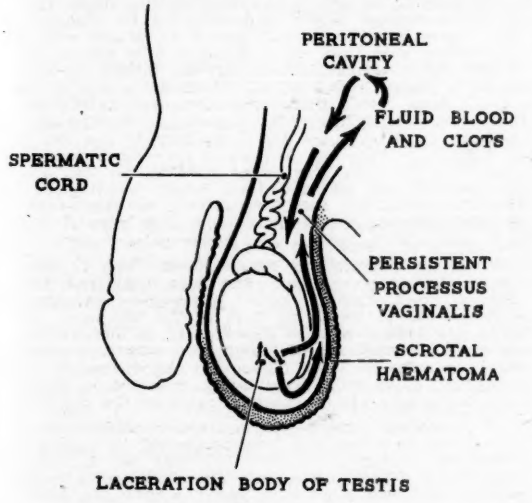

FIGURE I.

Showing hæmorrhage from a small tear in the body of the testis, and blood reaching the peritoneal cavity through a persistent processus vaginalis.

Comment.

No comparable case can be found in the literature. Watson (1948) refers to rupture of a vein of the sigmoid colon in a hernial sac causing hæmorrhage into the sac, but not into the peritoneal cavity.

The diagnosis was considered more likely to be injury to the bowel in the hernial sac or hæmoperitoneum from injury to other intraabdominal organs. Before the catheterization of the patient's bladder, a rupture of the bladder or urethra was considered a likely diagnosis. However, in spite of the uncertainty of the diagnosis, it was thought that the condition could be dealt with through an inguinal incision.

CASE II.—A widow, aged 45 years, a printer-typesetter, was admitted to the Canterbury District Memorial Hospital with a history of sudden onset of severe upper abdominal pain, sharp, persistent, referred to the back, and of vomiting of 24 hours' duration. Pain was also present in the lower right side of her chest. There was a previous history of long-standing duodenal ulcer, perforated duodenal ulcer and partial nephrectomy for renal calculi.

On examination, the patient was moderately shocked, pale and dyspnœic. The tongue was coated and dry. The abdomen was markedly tender and rigid. Rebound tenderness was present. The liver dullness was normal, and no masses were palpable in the abdomen. The bowel sounds were absent, and Murphy's sign was present. The pulse was regular at 100 per minute and the blood pressure was 190/120 mm. of mercury. No other abnormality was found on physical examination. A provisional diagnosis of perforated duodenal ulcer was made. Intravenous administration of fluids and gastric aspiration were commenced. The hæmoglobin value was 17·8 grammes per 100 ml. When the patient was examined by the Honorary Medical Officer, Dr. L. Abramovich, soon after her admission to hospital, the pain had greatly diminished, the blood pressure was 170/100 mm. of mercury and the pulse rate was regular at 110 per minute. One hour later the patient developed pain high up at the back on the right side of the chest. Two hours later she experienced a sudden increase in her pain, and became profoundly shocked and cyanosed and sweated; she complained of great thirst, and her radial pulse was impalpable. In spite of strenuous efforts at resuscitation with transfusion, nor-adrenaline and "Solucortef", the patient died twelve hours after her admission to hospital.

At the autopsy performed by Dr. M. Bullen, approximately 1·5 litres of fluid and clotted blood were found in the peritoneal cavity. Large blood clots extended over the supero-anterior and posterior surfaces of the liver down the right paracolic gutter and filled the pelvis. The superior surface of the right lobe of the liver had been completely disrupted by blood clot for an area about 3 in. in diameter, and blood clot separated the superior surface of the liver from the diaphragm. The portal tracts of the right lobe were filled with blood. The tracts of the left lobe were free of blood. The gall-bladder and bile ducts were distended by blood clot. The gall-bladder wall was thickened, and a small tear was present on the mucosa. On examination of sections, there was some blood in the wall of the gall-bladder, but this did not appear to be the source of the hæmorrhage. (See Figure II.) The pylorus was absent, and a superficial ulcer was found at the gastro-duodenal junction. No blood was present in the gastro-intestinal tract. The ovaries were small and fibrotic, with small follicular cysts into which hæmorrhage had occurred. Examination of the heart showed left ventricular hypertrophy, subendocardial petechial hæmorrhages and slight atheroma of the coronary arteries. There was moderate atheroma with calcification of the aorta.

On microscopic examination, all sections of the liver showed disruption with necrotic areas in the parenchyma and hæmorrhage in the portal tracts. Examination of sections of the gall-bladder in the region of the tear showed red cells and fibrin infiltrated by polymorphs. The muscle was fragmented and the epithelium lost. The kidneys showed patchy loss of glomeruli and hypertensive changes in the vessels.

Comment.

Theoretically this case would be classified as one of so-called spontaneous hæmoperitoneum or abdominal apoplexy, as no actual causative lesion for the hæmorrhage could be demonstrated. Brewer and Marcus (1948), in recording the published cases of intraabdominal apoplexy, found that in 12 of the 28 cases studied, no definite bleeding point could be demonstrated. They found that 14 of the 28 patients were reported to be suffering from arteriosclerosis. Other authors have also found these two conditions associated with intraperitoneal hæmorrhage (Woolf and Thomson, 1849; Ross, 1950; Sherwin and Gardiner, 1950). However, a number of cases in which hypertension or arteriosclerosis is definitely absent have been recorded. Brewer and Marcus found eight in their review. Woodruff reported the case of a normo-

tensive patient, aged 25 years, in which an aneurysm on an omental vessel ruptured. Jurischa and Vacarro (1952) recorded the case of a girl, aged two years, with spontaneous hæmoperitoneum for which no source of hæmorrhage could be found.

Ellis, Griffith and MacIntyre (1958) suggest that in some young patients, not suffering from hypertension or arteriosclerosis, when the site of bleeding is not obvious, the hæmorrhage is from spontaneous rupture of a congenitally defective vessel wall, comparable to a berry aneurysm occurring in the cerebral vessels. They quote Nevin and Williams (1937), who described the rupture of an aneurysm of the splenic artery with multiple aneurysms on the branches of the circle of Willis, and a subarachnoid hæmorrhage from a berry aneurysm on the circle of Willis, associated with a massive hæmoperitoneum of uncertain origin. Therefore they consider that arteriosclerosis and congenital vascular defects probably explain most cases of abdominal apoplexy when this is not due to some more obvious cause, and that the failure to find the bleeding site is due to the fact that it may be of microscopic dimensions and so defies diagnosis.

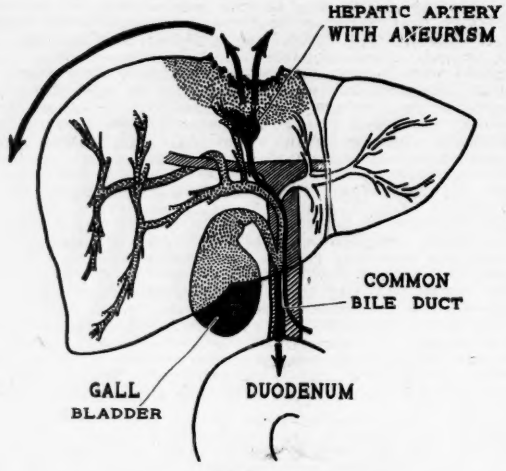

FIGURE II.

Showing rupture of intrahepatic aneurysm into a bile duct, and subsequent rupture through the superior surface of the liver causing hæmoperitoneum. Note the blood through the right lobe bile ducts, gall-bladder and common bile duct. There is no blood in the duodenum or left lobe ducts.

In the case under discussion, although no actual bleeding site was demonstrated, the evidence strongly points to the rupture of an arteriosclerotic aneurysm on an intrahepatic branch of the right hepatic artery (or, less likely, a congenital aneurysm associated with hypertension) into a major bile duct, and then the disruption of the liver tissue and the eventual rupture through the superior surface of the liver and into the peritoneal cavity with fatal hæmoperitoneum (see Figure II). The bleeding was obviously of the intrahepatic type; none of the other causes of intrahepatic biliary tract hæmorrhage were found.

The patient was hypertensive, and on her admission to hospital, in spite of her state of apparent shock, her blood pressure was still 190/120 mm. of mercury. The sequence of events appears to have been rupture of the aneurysm into, perhaps, the caudate branch of the right hepatic duct, with bleeding down the biliary tract and severe pain in the right hypochondrium and through to the back, similar to biliary colic. Very soon the continued bleeding disrupted the liver tissue, and the blood forced its way onto the superior surface in the region of the bare area and subsequently through the peritoneum, with fatal intraperitoneal hæmorrhage (Figure II). The branches of the bile ducts, hepatic artery and portal vein closely cling together in their course through the liver substance (Hobsley, 1958).

Most cases of bleeding into the biliary tract present with hæmatemesis and/or melæna. The resultant hæmatemesis or melæna is often severe and persistent, and may occur repeatedly over a period of months (Gordon Gordon-Taylor, 1943; Kerr, Marsh and Gould, 1950; McGregor, 1952). Some of these patients have been submitted to operation up to four times; some have had partial gastrectomy and even repeated exploration of the bile duct, blood clot being found on each occasion, but the site of bleeding was not demonstrated *ante mortem*.

It may be worth while mentioning at this juncture that at operations for persistent severe hæmatemesis or melæna, if no lesion is found in the stomach or duodenum before embarking on "blind" partial gastrectomy, it is extremely important to search for and exclude other lesions, including bleeding from or into the biliary passages. However, it is interesting to note in this case that although the bile ducts and the gall-bladder were quite distended with blood clot, no free blood was found in the lumen of the alimentary tract. It appears that a spasm of the sphincter of Oddi had occurred, and that perhaps the early release of the blood through the superior surface of the liver and into the peritoneal cavity, with rapid death, prevented the creation of sufficient pressure to force the blood into the gastro-intestinal lumen.

CASE III.—The notes on this case have been supplied by Dr. M. Matheson.

A female patient, aged 20 years, was examined at 9 p.m. on June 17, 1959, in a shocked condition, with vaginal bleeding, tenderness and pain in the lower part of the abdomen. Investigation of her menstrual history showed that she had a normal cycle of 28 days with the menstrual periods lasting four or five days. The last normal menstrual period had occurred on February 25, 1959. There was no normal period in March and April. The patient said that she had taken pills and purgatives on several occasions because of the missed periods. On April 30 there was vaginal bleeding, which continued for 15 days. Then there was none for two days, but this break was followed by "shows" until May 30, with floodings on May 5 and 12. From May 30 she lost heavy clots for four days and had slight pain for a week. From June 5 to 11 there was heavy bleeding, no loss occurred on June 13 and 14, and then heavy bleeding occurred again on June 15, with severe pain in the lower part of the abdomen. On June 17 she had copious bleeding with clots and a good deal of pelvic pain.

When the patient was examined on June 17, she was losing clots per vaginam. She was pale and shocked, with a rapid, thready pulse. Tenderness and guarding were present in the lower part of the abdomen. At that stage a coherent history was difficult to obtain. A diagnosis of ruptured ectopic pregnancy was made. After a blood transfusion, and consequent improvement in her condition, a vaginal examination revealed a closed os with tenderness and a probable mass in the right fornix.

At 2 a.m. on June 18, her general condition was much better, and a laparotomy was performed through a lower abdominal mid-line incision by Dr. M. Matheson at Bankstown District Hospital. The findings at operation were as follows. Free dark blood with some dark clots was found in the peritoneal cavity. There was dark blood clot in both Fallopian tubes, more in the right than in the left. These clots were "milked" out of the fimbriated end of the tubes, and both tubes were found to be normal. The right ovary contained a simple cyst containing clear fluid. The cyst was removed. The left ovary was normal. The uterus was bluish in colour, slightly enlarged and globular. Laparotomy was followed by dilatation and curettage. The os was closed, and as dilators were introduced dark blood oozed from the uterus as though under pressure. Further old clot was removed during curettage. Endometrial tissue sent for pathological examination was reported as being in the "late premenstrual phase".

Convalescence was uneventful. On August 19 the patient was well, and had had two normal menstrual periods since operation. Vaginal examination revealed a small, tender cystic mass in the left fornix. This was considered to be due to resolving blood clot, which had probably

passed up the Fallopian tube during dilatation and curettage.

Comment.

That this was a true case of hæmoperitoneum is shown by the abdominal symptoms and signs and by the amount of blood found in the peritoneal cavity at operation, although it would seem that the patient's state of shock was produced perhaps more by the prolonged and heavy vaginal bleeding than by her degree of hæmoperitoneum.

It would appear, then, from this patient's history that the closure of the uterine cervix by old blood clot or other debris may offer sufficient resistance to cause the back flow of a fairly large quantity of blood through the Fallopian tubes into the peritoneal cavity. Once the intrauterine pressure had reached a certain level, then further heavy vaginal bleeding followed (Figure III).

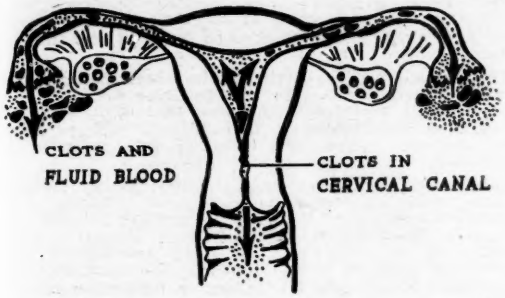

FIGURE III.

Showing clots in the cervical canal, and temporary obstruction to the outflow of blood, with resultant retrograde bleeding from the fimbrial ends of the Fallopian tubes.

In the literature consulted, the only uterine hæmorrhage spilling back into the peritoneal cavity through the fimbrial ends of the Fallopian tubes mentioned is that associated with congenital abnormalities causing hæmatocolpos, hæmatometra and bilateral hæmatosalpinx. Dumoulin (1953) reported one such case, in which 1·5 litres of old blood was milked out after the vaginal defect had been incised. Some blood had leaked out into the peritoneal cavity through the fimbrial ends of the Fallopian tubes. This patient subsequently became pregnant and went on to a normal delivery. Dumoulin refers to a personal communication from another gynæcologist who had found hæmoperitoneum produced in the same way.

It would appear that the treatment in the case under discussion is laparotomy and gentle milking of clots out of the Fallopian tubes, removal of blood clot from the peritoneal cavity, and dilatation and curettage to arrest the bleeding and to remove any mechanical obstruction to the outflow of blood from the uterine cavity.

There was no evidence of any congenital abnormality in the genital tract of this patient which could have prevented the free outflow of blood from the uterine cavity. That small quantities of blood frequently spill back into the peritoneal cavity through the Fallopian tubes after uterine bleeding is well known. Retrograde menstruation is often observed in the course of surgical operations, and Tagart (1959) quotes Sampson (1921), who states that endometriosis of one pelvic organ or another occurs in 10% to 20% of women between the ages of 30 years and the menopause. In the great majority of cases, of course, the condition is symptomless. However, it seems distinctly unusual for large amounts of blood, sufficient to produce obvious signs and symptoms of hæmoperitoneum, to spill back into the peritoneal cavity following uterine hæmorrhage.

SUMMARY.

1. Three cases of hæmoperitoneum are studied, each being of rare ætiology.

2. The first case was one of hæmoperitoneum caused by bleeding from a testicular laceration, the blood gaining access to the peritoneal cavity through a persistent processus vaginalis. The surgical treatment consisted of arresting the hæmorrhage, removing the hernial sac and repair of the inguinal canal defect.

3. The hæmoperitoneum in the second case was caused by the spontaneous rupture of a probable aneurysm of an intrahepatic branch of the right hepatic artery into a bile duct, with subsequent fatal rupture through the superior surface of the liver.

4. The causes of spontaneous hæmoperitoneum or abdominal apoplexy are discussed. It would seem that arteriosclerosis and congenital vascular defects are probably the cause in most of these cases, and the failure to find the actual bleeding site is due to the fact that it may be of microscopic dimensions.

5. Reference is made to aneurysm of the hepatic artery, which presents clinically as the triad of pain, jaundice and gastro-intestinal hæmorrhage. Ligation of the hepatic artery proper just before it divides to enter the liver distal to the gastro-duodenal and right gastric branches would seem justifiable in aneurysms involving the main hepatic artery. In intrahepatic aneurysms, ligature of one of the branches of the hepatic artery at the hilum is a possibility. Penicillin should be administered after these procedures. Other successful forms of treatment recorded are wrapping of the aneurysm with "Cellophane" and dicetyl phosphate and obliterative endoaneurysmorrhaphy. The suggestion is made that some aneurysms of the hepatic artery in its extrahepatic portion may be suitable for treatment by acrylic investment.

6. The escape of blood from the uterus via the Fallopian tubes following a probable abortion was the cause of the hæmoperitoneum in the third case. It would appear that blockage of the cervical canal by blood clot resulted in a large amount of blood being forced back along the Fallopian tubes into the peritoneal cavity. The surgical treatment consisted of laparotomy, expression of blood clots from the Fallopian tubes and curettage.

7. Some other causes of hæmoperitoneum, both usual and unusual, are listed.

ACKNOWLEDGEMENTS.

My thanks are due to Mr. C. E. Winston and Mr. H. K. Porter for their advice in the preparation of this publication; to Dr. L. Abramovich and Dr. M. Matheson for permission to publish their cases (Cases II and III); to Dr. A. H. Sadler, Medical Superintendent of the Canterbury District Memorial Hospital, and Dr. J. Hooper, Medical Superintendent of the Bankstown District Hospital, for permission to publish these three cases; to Dr. M. Bullen and Dr. A. Kertez for the pathologists' reports; and to Mr. B. Dumphy for the preparation of the diagrams.

ADDENDUM.

Since submission of this article for publication, another patient has been treated for hæmoperitoneum, in this case resulting from the disruption of a necrotic parietal peritoneal secondary tumour. The primary tumour, an enormous leiomyosarcoma, had been removed 15 months previously.

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AN ATTEMPT TO DEMONSTRATE IMMUNOLOGICAL DIFFERENCES BETWEEN THE SERA OF NORMAL AND OF CARCINOMA-BEARING MICE.

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A MALIGNANT TUMOUR growing in a vertebrate may be expected to produce immunologically detectable effects in the circulating plasma, either by the abnormal penetration into the blood-stream of antigenic substances deriving from the tumour itself, or by the tumour's having an abnormal influence upon the functions of organs or tissues which do not normally release their products into the circulation.

Darcy (1955) immunized rabbits with the sera of rats bearing the transplantable Walker carcinoma and looked for precipitin reactions by the Ouchterlony gel diffusion technique (Oudin, 1952). He found a line indicating a precipitin reaction between the immune rabbit serum and the cancer-bearing rat serum which did not occur with normal rat serum. However, he obtained the same reaction with serum taken from some rats which had been tightly bandaged around the abdomen and which had not been fasted before bleeding.

In subsequent work, Darcy (1957) reported on other precipitin lines which he had obtained both with normal and with cancer sera, but exclusively with neither. One antigen in particular, a mucoprotein present in normal rat serum, appeared to increase greatly in concentration while a tumour was developing, or when non-cancerous rats were growing or regenerating their tissues. He referred to similar changes which he had found in the sera of human patients with carcinoma, but these, or something very like them, could also be observed in sera from some patients with non-neoplastic diseases.

We have immunized rabbits with the sera of mice bearing the transplantable Ehrlich ascites mouse carcinoma. Mice with other irritant lesions, and pregnant mice, were used as controls. We looked particularly for the appearance of a specific or characteristic carcinoma serum antigen.

Materials and Methods.

The experiments were carried out as follows.

White mice (males, except for the pregnant controls) were taken from a single strain which has been maintained for general use in this Institute for the past 25 years. They were bled by cardiac puncture under chloroform anæsthesia after 12 hours' fasting. Forty-seven rabbits, from a mixed stock also kept in the Institute, were immunized with the mouse sera.

The Ehrlich ascites carcinoma has been maintained as a virus growth medium in this Institute for some years by fortnightly transfer in the peritoneal cavities of mice. If injected subcutaneously into mice it will produce a solid tumour, and it was used in this form in this experiment.

Serum was separated from blood samples taken by cardiac puncture from normal mice (N.M.S.), from cancer-bearing mice (C.M.S.) at various stages after transplantation of the tumour, from normal pregnant mice, from mice having had fresh mouse-liver saline suspensions injected intraperitoneally five days previously, from mice with single intramuscular turpentine abscesses (0·1 ml. of a 10% saline suspension of turpentine), and from mice with turpentine peritonitis (same dose as above). Thirty to 50 mice in each category were required to produce sufficient serum, which was pooled, and injected into rabbits while fresh. The remainder was stored at —20° C., for use in the antigen wells of the gel-diffusion plates.

Commercially prepared "Difco Bacto-Adjuvant", complete (Freund), was used in equal proportions with the various mouse sera for intra-muscular inoculation.

Rabbits were immunized initially with 0·5 ml. of mouse serum injected intravenously and with 0·5 ml. of serum-adjuvant mixture injected intramuscularly at five-day intervals until their immune response had become maximal, which was usually in 20 to 30 days. An interval of at least five days was always allowed after an injection of antigen before a rabbit was bled. Rabbit serum was stored at —20° C.

Powdered "Difco-Bacto" agar (1%) was dissolved in sterile, normal saline; it was steamed and filtered, and "Merthiolate" (1/10,000 solution) was added. Amounts of 25 ml. were poured in 8 cm. Petri dishes and left overnight at 4° C. Wells were cut 1·3 cm. apart in the agar in the required patterns, and the plates were dried at 37° C. for 30 minutes. The antibody and antigen wells were filled with rabbit antisera and mouse sera respectively, the rabbit sera being diffused undiluted against the various categories of mouse sera both neat and diluted 1:2, 1:4, 1:8, 1:16, 1:32. The plates were incubated at 37° C. for three to eight days while the precipitin patterns developed. They were photographed by direct printing of the agar plates on sensitive paper in a beam of light from a photographic enlarger, in which the source lamp had been moved slightly off centre to give an oblique incidence of the beam on the precipitin lines. We obtained a printed image 1·4 times the dimensions of the plates. For reproduction in this paper, prints were rephotographed with black-outlined labels placed within the shadows of the wells.

Results.

All the mouse sera used were antigenic in the rabbit, and after the usual interval stimulated the production of precipitins which gave lines of varying densities, thicknesses and relative positions when antigen-antibody reactions between rabbit and mouse sera were examined by Ouchterlony agar-gel diffusion. The optimum dilution of mouse serum for display of the maximum number of discrete precipitin lines was generally 1:8. No difference was found between mouse serum and mouse plasma as antigens.

[1] In receipt of a grant from the National Health and Medical Research Council of Australia.

When the precipitin reactions of C.M.S. and N.M.S. were compared, no unique precipitin line similar to that found by Darcy in his rat experiment (Darcy, 1955), was observed with immune sera from any of 25 rabbits inoculated with C.M.S. Some five to nine lines usually appeared (mean 6·6); but when a rabbit anti-C.M.S. formed precipitin lines with C.M.S. in agar gel, it always formed identical lines with N.M.S. at the same dilutions (Figure I). Antigen-titration plates were set up, and these gave no indication of any quantitative difference between comparable serum antigens of C.M.S. and N.M.S., nor was any unique "normal" line present only with N.M.S.

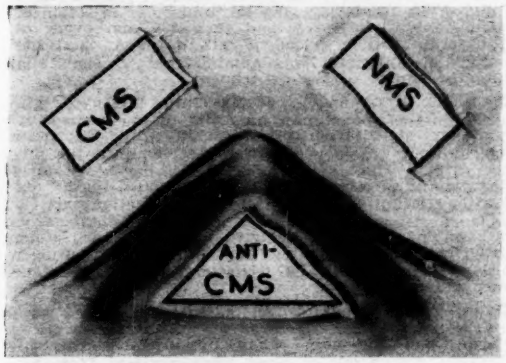

FIGURE I.
Eight distinguishable lines.

At the same time, one definite difference between C.M.S. and N.M.S. was observed. When their respective antigenicities in the rabbit were compared, N.M.S. did not stimulate the production of as many distinct precipitating antibodies as did C.M.S., to judge by the distinguishable precipitin lines (Figure II), the number varying from three to seven (mean 4·4) with sera from 14 immunized rabbits. Notwithstanding this, any N.M.S. which had failed to stimulate as many precipitins as C.M.S. *in vivo* would always give the extra lines when tested with an anti-C.M.S. *in vitro*.

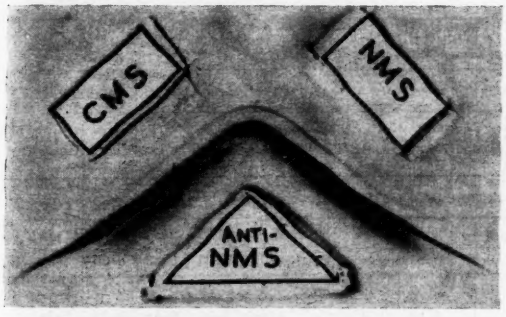

FIGURE II.
Five distinguishable lines.

Further work then showed that sera from mice with turpentine abscesses, turpentine peritonitis or intraperitoneal mouse-liver suspensions, or pregnant mice, all behaved in the rabbit in the same way as C.M.S. Eight rabbits were immunized, two with each of the above-mentioned kinds of "acute phase" mouse sera, and these stimulated a larger number of precipitins than did N.M.S.; but the precipitins from each rabbit reacted in the diffusion plates with C.M.S., N.M.S., and "acute phase" sera indistinguishably.

We have therefore failed to demonstrate any specific or characteristic "cancer-change" in the antigens of the sera of carcinoma-bearing mice.

Discussion.

The appearance of free malignant cells in the blood-stream is now known to be a more frequent accompaniment of human carcinoma than was suspected in the past (*Pruitt et alii, 1958; Salgado et alii, 1959*). Moreover, Makari (1955), using the Schultz-Dale technique, has claimed to have demonstrated the presence of a characteristic carcinoma antigen in the sera of human patients, and his work has been confirmed by Burrows (1958). Again, tissue-specific antigens are known to exist, and as epithelial tissue does not transgress its basement membrane and penetrate to the mesodermal blood spaces except by malignant carcinomatous invasion, in such a condition epithelial antigens may well appear in the blood.

For such reasons we hold that an immunological approach to the serum detection of carcinoma may eventually succeed, and we do not publish our present negative experimental results in the belief that others who have reported characteristic serum antigens in association with human or animal carcinoma are mistaken. Nevertheless, even if a unique cancer antigen had been demonstrated in our mice, these would have been incomplete models of human patients with autogenous carcinoma, for the Ehrlich ascites tumour, being transplanted, may release specific antigens related, not to its epithelial or malignant status, but to its origin in an antigenically different animal.

The increased antigenic range of mouse-carcinoma sera injected into rabbits which we noted was not a cancer-specific quality, for it was present in the sera of mice in other abnormal states, and was evidently in the nature of an "acute phase phenomenon", probably related only to trauma or gross physiological disturbance in general. This difference in antigenic potency may have been caused by an increase in the concentration of normal serum antigens in the diseased mice, the ordinary levels being too low to stimulate an antibody response in the rabbit. If this was so, it was curious that the precipitin reactions in agar gel were equally strong when cancer-bearing or other "acute phase" mouse sera were compared with normal mouse sera at the same dilutions, for this suggested that there was little difference between them so far as the concentration of antigens reacting in the agar was concerned. However, a simple agar-gel diffusion titration technique assessed by ordinary inspection may not give accurate quantitative results when the antigens remain uncharacterized.

Alternatively, the differences may have been caused by some substances which appeared in normal mouse sera only as complex haptens, or in a state in which they were very rapidly eliminated from the rabbits bodies, but which were released into the blood-stream of the diseased mice in a complete antigenic form. This seems the best explanation of our results as they stand.

Summary.

1. An attempt was made to demonstrate the presence of a cancer-specific antigen in the sera of carcinoma-bearing mice, using the Ouchterlony agar-gel diffusion technique.

2. No such antigen was found.

3. Certain differences in antigenicity between the sera of normal mice and the sera of mice with cancer or in a state of gross physical disturbance suggested that antigens present only in haptenic or simplified molecular form in the normal sera were to be found as complete antigens in the blood of the abnormal mice.

Acknowledgement.

We are grateful to Dr. J. Orde Poynton for advice and discussion during the progress of this work.

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SERUM LEVELS OF OXYTETRACYCLINE FOLLOWING INTRAMUSCULAR ADMINISTRATION OF A PRECONSTITUTED SOLUTION.

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RECENT experiments with preconstituted oxytetracycline solutions indicate that intramuscular administration of this antibiotic can now be achieved without severe local reaction and without loss of potency, during treatment, of the original solution. Hammer *et alii* (1959) have described investigations carried out with an ethanol-ammonium magnesium salt of oxytetracycline, while Weinstein *et alii* (1959) have shown that a solution of this salt in an 80% propylene-glycol-water vehicle is stable, effective and well tolerated.

The purpose of the present investigation was to determine serum levels of oxytetracycline following the administration of a preconstituted solution to healthy volunteers and to arrive at an adequate dosage schedule for this preparation.

Materials and Methods.

Twelve third-year medical students were selected from a number of volunteers. Apart from regular attendance for injections and venepunctures, all subjects continued with their normal routine, which included lectures, ward rounds and various athletic pursuits.

The material used consisted of 250 mg. of oxytetracycline as the ethanolammonium magnesium salt, with 2% lignocaine in an 80% aqueous propylene glycol vehicle. The injection was supplied in 2 ml. ampoules of amber glass, sealed over an inert atmosphere. Each volunteer received 250 mg. of oxytetracycline by intramuscular injection every 24 hours for three doses, and then 250 mg. every other day over a further period of six days. A total of 1·5 grammes of antibiotic was administered to each subject during the course of the experiment.

Injections were given deeply into alternate gluteal muscles, in the upper outer quadrant of the buttock. After preliminary sterilization of the skin with chlorhexidine in spirit, a 21 gauge needle was inserted into the muscle mass with a single thrust. A 2 ml. dry-heat sterilized syringe containing the solution was attached to the needle, and after precautionary aspiration, the injection was slowly completed. All syringes were filled by attaching a wide-bore cannula, which was inserted into the opened ampoule. In this way, contamination of the injection needle with solution was avoided and irritation of the subcutaneous tissues did not occur.

Serum levels of oxytetracycline were estimated at four and 24 hours after each injection. Assays were also performed on the days when no injection was given. Approximately 10 ml. of blood were removed from a vein in the ante-cubital fossa, and serum levels were estimated by the plate diffusion technique of Grove and Randall (1955).

Results.

No subject reported any toxic reactions during the course of injections. One volunteer recalled some looseness of the motions when directly questioned, but this could not be definitely associated with the antibiotic. All subjects agreed that the injections themselves were painless. No redness or induration of the injection site was noted in any of the volunteers. However, assessment of post-injection pain and discomfort was exceedingly difficult owing to a wide variation in the pain threshold. At one extreme, a very phlegmatic subject appeared totally unconcerned throughout the course of the experiment, while

TABLE I.

Individual Serum Levels of Oxytetracycline in 12 Volunteers.

Subject.	Weight. (Pounds.)	Day I: 4 Hours.	Day II.		Day III.		Day IV.		Day V.		Day VI.		Day VII.		Day VIII.		Day IX.		Day X: 24 Hours.
			24 Hours.	4 Hours.	24 Hours.	4 Hours.	24 Hours.	4 Hours.	24 Hours.	4 Hours.	24 Hours.	4 Hours.	24 Hours.	4 Hours.	24 Hours.	4 Hours.	24 Hours.	4 Hours.	
1	133	1·30	0·48	1·12	0·48	2·10	0·76	0·42	0·24	1·70	0·90	0·52	—	1·40	1·10	0·60	0·29	1·56	0·84
2	154	0·90	0·42	0·95	0·54	1·68	0·56	0·41	0·20	0·92	0·60	0·40	—	1·04	0·80	0·56	0·38	1·24	0·64
3	182	0·76	0·34	0·90	0·52	1·36	0·56	0·38	0·28	0·72	0·32	0·32	—	0·90	0·80	0·62	0·30	1·24	0·60
4	200	0·80	0·42	0·52	0·42	2·00	0·60	0·42	0·28	0·92	0·54	0·50	—	1·28	0·76	0·50	0·27	1·12	0·62
5	180	0·76	0·38	0·82	0·52	1·70	0·76	0·34	0·26	1·30	0·50	0·50	—	1·08	0·90	0·44	0·34	1·00	0·66
6	147	1·08	0·48	1·00	0·54	1·90	0·74	0·28	0·28	1·00	0·72	0·48	—	1·22	1·28	0·62	0·44	1·08	0·80
7	147	1·20	0·46	1·16	0·54	1·40	0·64	0·41	0·30	0·94	0·66	0·52	—	1·28	0·80	0·70	0·23	1·24	0·65
8	144	1·00	0·42	1·12	0·68	1·70	0·76	0·42	0·26	1·00	0·70	0·52	—	1·54	0·90	0·62	0·32	1·20	0·64
9	177	0·70	0·42	0·70	0·48	1·40	0·54	0·41	0·24	1·20	0·62	0·46	—	1·00	1·00	0·60	0·20	0·94	0·62
10	147	0·54	0·49	1·02	0·54	1·68	0·80	0·52	0·28	1·50	0·80	0·60	—	1·40	1·00	0·64	0·26	1·24	0·61
11	143	0·96	0·46	1·12	0·50	1·80	0·60	0·52	0·30	—	0·70	0·50	—	1·28	0·90	0·44	0·32	1·04	0·56
12	185	0·65	0·40	0·69	0·50	1·04	0·60	0·44	0·28	0·90	—	0·48	—	0·80	0·84	0·54	0·30	1·04	0·60
Mean values	—	0·88	0·43	0·92	0·52	1·64	0·66	0·41	0·26	1·08	0·64	0·48	—	1·14	0·84	0·57	0·30	1·16	0·65

two hypersensitive individuals complained of severe post-injection discomfort and also pain arising from repeated venepunctures. The general impression gained was that the injections were well tolerated, the fact being borne in mind that the subjects were not at rest in bed and that the injected muscle masses were continually exercised.

The serum levels obtained in individual subjects are shown in Table I and the mean serum levels are presented graphically in Figure I. Owing to an accident in the laboratory, the 24-hour levels for the seventh day were not determined.

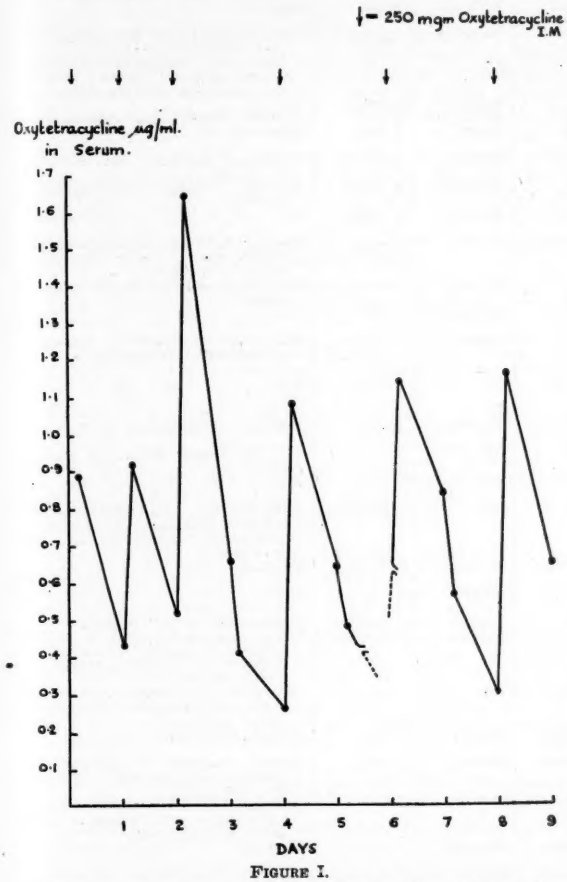

FIGURE I.

Mean serum levels of oxytetracycline in 12 experimental subjects.

An interesting cumulative effect following three successive daily injections is shown. When dosage is reduced to 250 mg. on alternate days, detectable serum levels are still obtained 48 hours after the previous injection.

Discussion.

Although the 48-hour levels obtained with intermittent therapy are low on the scale of therapeutic usefulness, the table of sensitivity of various organisms to oxytetracycline (Welch, 1954) indicates that at least some infections could be treated by this regimen, particularly when in-vitro sensitivity tests are available. However, in most cases a single daily injection of this preparation, which is well tolerated and free from toxicity, would seem preferable to resorting to alternate-day therapy after three successive daily injections. The low 48-hour serum levels obtained with intermittent injections carry with them the risk of rapidly developing bacterial resistance, and this regimen does not seem justifiable except in carefully selected cases.

Summary.

Twelve volunteers received a preconstituted solution of oxytetracycline by intramuscular injection on three consecutive days and on alternate days thereafter.

The injections were well tolerated and there were no toxic reactions.

A cumulative effect was demonstrated during the period of daily injections, and serum levels were still demonstrable at 48-hour intervals during intermittent therapy.

The clinical usefulness of resorting to intermittent treatment after three consecutive injections is briefly discussed.

Acknowledgements.

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PRELIMINARY OBSERVATIONS ON THE USE OF IMIPRAMINE IN THE TREATMENT OF DEPRESSION.

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IMIPRAMINE, an iminodibenzyl derivative, is structurally related to chlorpromazine and is sedative in most of its effects in animals. Because of this relation it was first investigated for any chlorpromazine-like activity in 1954 by Kuhn in Switzerland, when specific anti-depressive effects were noted.

In three years Kuhn (1957, 1958) treated 500 patients suffering from various psychiatric disorders, the best results being obtained in endogenous depression. He states that success can be expected in 75% of such cases. In reactive depression results were less, but still significant.

Subsequent workers have largely confirmed these findings. Kielholz and Battegay treated 69 patients with severe depression and found that 67% were improved. Lehmann *et alii* (1958) reported improvement in 60% of 84 cases in which depression was a prominent feature. Delay *et alii* (1959) treated 137 patients with depressive disorders; 75% of those with recurrent depressions recovered or showed great improvement. In involutional melancholia, 67% of patients responded to the same degree. Lemere in Seattle, on the other hand, after using imipramine on a group of 137 out-patients over a period of two years, has found it "disappointing", only 22 of the 137 receiving transient benefit.

Most workers are agreed that imipramine is ineffective in the treatment of schizophrenic depression or depression associated with neurosis or psychopathy.

Method.

All the 35 patients in this series were adult males treated at Rockingham, Kew, in the six months commencing June, 1959, all but four being in-patients for at least the first four weeks of treatment with imipramine.

TABLE I.

Case.	Age. (Years.)	Diagnosis.	Previous Treatment.	Degrees of Improvement with Previous Treatment.	Improvement with Imipramine.	Time Elapsed Before Imipramine Effect Noted.	Side Effects and Comments.
1	42	Recurrent depression.	Iproniazid, phenos.,[1] amphets.[1]	Slight.	Moderate.	1 week.	Nil. Treated as out-patient.
2	63	Endogenous depression.	E.C.T.[1]	Slight.	Moderate.	1 week.	Relapsed in 1 month, imipramine ceased and E.C.T. recommenced. Sweating.
3	40	Schizoid depression.	E.C.T.	Moderate.	Marked.	1 week.	Generalized pruritus wiyhout rash. Sweating. Both subsided in 3 weeks.
4	40	Reactive depression in schizoid personality.	E.C.T.	Moderate.	Moderate.	2 weeks.	Nil.
5	45	Recurrent depression and chronic alcoholism.	Phenos., E.C.T.	Slight.	Moderate.	1 week.	Nil. Manipulation of environment and identification with Alcoholics Anonymous were factors contributing to improvement. Country patient, not followed-up after discharge.
6	62	Endogenous depression.	Amphets., phenos.	Slight.	Marked.	1 week.	Sweating.
7	56	Endogenous depression.	E.C.T., iproniazid.	Slight.	Marked.	1 week.	Sweating; treated as out-patient.
8	56	Recurrent depression in inadequate personality.	Phenos., amphets.	Slight.	Slight.	1 week.	Sweating.
9	40	Neurotic depression.	E.C.T., phenos., amphets.	Slight.	Marked.	1 week.	Sweating; pruritus; both subsided in 3 weeks.
10	54	Endogenous depression.	Amphets., phenos.	Slight.	Moderate.	2 weeks.	Sweating; pruritus; both subsided in 3 weeks.
11	40	Recurrent depression in schizoid personality.	Amphets., phenos.	Slight.	Moderate.	3 weeks.	Nil.
12	38	Schizophrenic depression.	E.C.T., phenos.	Moderate.	Nil.	1 week.	Became hypomanic and unmanageable. Settled down 4 weeks after withdrawal of imipramine.
13	60	Agitated endogenous depression.	Amphets., phenos.	Nil.	Nil.	——	Nil. Imipramine withdrawn after 1 month.
14	60	Endogenous depression with alcoholism.	E.C.T., amphets., phenos.	Moderate.	Moderate.	1 week.	Nil.
15	44	Recurrent depression with alcoholism in inadequate personality.	E.C.T., amphets., phenos.	Slight.	Slight.	2 weeks.	Nil; ceased imipramine on discharge; relapsed with suicidal attempt.
16	36	Reactive depression in inadequate hysterical personality.	E.C.T., amphets., iproniazid, phenos.	Moderate.	Nil.	——	Nil.
17	47	Schizophrenic depression.	E.C.T., amphets., phenos.	Slight.	Moderate.	1 week.	Pruritus; subsided in 2 weeks.
18	44	Neurotic depression with alcoholism.	E.C.T., phenos.	Slight.	Nil.	——	Nil; imipramine withdrawn after 5 weeks.
19	45	Recurrent depression.	E.C.T., amphets., phenos.	Moderate.	Moderate.	1 week.	Nil.
20	35	Recurrent depression in psychopathic personality.	Amphets., phenos.	Slight.	Slight.	2 weeks.	Environmental manipulation and transient enthusiasm for Alcoholics Anonymous contributed to improvement.
21	53	Recurrent depression.	E.C.T., amphets., iproniazid.	Moderate.	Marked.	2 weeks.	Sweating.
22	62	Endogenous depression initiated by reserpine.	Amphets., phenos.	Slight.	Marked.	2 weeks.	Nil.
23	64	Endogenous depression.	Amphets., phenos.	Slight.	Marked.	2 weeks.	Nausea, relieved by "Bellergal".
24	42	Recurrent depression with anxiety.	Amphets., meprobromate.	Nil.	Marked.	3 weeks.	Ceased imipramine after 1 month because of accommodation defect. Relapsed. Recovered on recommencing imipramine.
25	42	Recurrent depression.	E.C.T., amphets.	Moderate.	Nil.	——	Complained of vertigo and nausea, would not persist with imipramine after 2 months.
26	48	Recurrent neurotic depression.	Phenos.	Moderate.	Marked.	10 days.	Postural hypotension.
27	38	Reactive depression.	E.C.T.	Moderate.	Marked.	1 week.	Usually dyspeptic, he claimed imipramine made this worse. Relieved by "Bellergal".
28	42	Recurrent depression.	E.C.T.	Moderate.	——	——	Complained of bizarre nocturnal visual hallucinations which ceased on withdrawal of imipramine.
29	41	Recurrent depression in schizoid personality.	E.C.T., phenos.	Moderate.	Moderate.	1 week.	Sweating.
30	68	Manic-depressive.	E.C.T., iproniazid, phenos.	Moderate.	Slight.	2 weeks.	Nil.
31	38	Recurrent depression.	E.C.T., phenos.	Moderate.	Moderate.	2 weeks.	Sweating.
32	39	Reactive depression.	Phenos.	Slight.	Nil.	——	Nil; imipramine withdrawn after 4 months.
33	44	Endogenous depression.	E.C.T., amphets., phenos.	Moderate.	Moderate.	2 weeks.	Nil; partial remission with E.C.T., further improved with imipramine.
34	48	Neurotic depression in hysterical personality.	E.C.T., amphets., phenos.	Slight.	Slight.	2 weeks.	Complained of nausea.
35	43	Chronic depression in schizoid personality.	Phenos., amphets.	Nil.	Marked.	2 weeks.	Nil.

[1] Phenos., phenothazine derivatives; amphets., amphetamines; E.C.T., electro-convulsive therapy.

All patients but one had had previous treatment in hospital for psychiatric illness, many having had multiple admissions. Most of these patients had histories extending over the past 10 to 15 years, and had been treated with electroconvulsive therapy and tranquillizers, with varying degree of success.

Cases were selected from consecutive admissions in which depressive symptoms were major presenting features. Criteria of improvement were based on the pooling of patient's subjective impressions, and on nursing and occupational therapy staff reports, the final decision being made by the consultant psychiatrist and myself. The drug was ordered for the patient without special comment, and he was subjected to the usual therapeutic régime at Rockingham. No control investigation was attempted, for obvious reasons.

The following dosage routine was used: one 25 mg. tablet was given three times a day for three days, then two tablets were given three times a day for one week, and this was increased to three tablets three times a day

in some cases when necessary; the maintenance dose was one or two tablets three times a day.

Results.

Table I lists diagnosis, previous treatment, response to previous treatment, time taken before the effect of the imipramine was seen, degree of improvement noted, side effects and other relevant comments. From the table, the following results may be stated: there was marked improvement in 11 cases; moderate improvement occurred in 12 cases; slight improvement was noted in five cases; no change was observed in seven cases.

Comments.

Bearing in mind the many significant variables involved in assessing the effects of psychopharmaceutical agents on behavour (Sherman) and the difficulties in controlling them, I believe that only those cases in which improvement was marked can fairly be claimed as successes for this drug at this stage.

Results from such a small series give no reliable guide to the precise indications for imipramine, but my experience suggests that it is worthy of trial in all types of depression.

The following three brief case histories are typical of patients showing marked improvement:

CASE 26.—A successful business executive, aged 48 years, with a history of 15 years' recurrent, moderately severe depression, was seen in a stage of deep depression with suicidal ruminations, insomnia and psychomotor retardation. After two weeks of imipramine therapy there was a feeling of buoyant optimism and "freedom from depression for the first time in many years".

CASE 35.— A highly intelligent clerk (I.Q. 140) had been treated with psychotherapy and drugs as an out-patient for some years without success. He complained of depression and difficulty in interpersonal relationships, and his condition was diagnosed as chronic depression in a schizoid personality. When he was examined one month after the commencement of imipramine therapy, a marked improvement in affect was apparent.

CASE 24.—The patient was a man, aged 42 years, suffering from chronic anxiety and depression. Marked improvement in mood and warmer social contacts were reported after two weeks' out-patient treatment with imipramine. After two months he was admitted to hospital showing agitation, dissociation and depersonalization. It appeared that he had stopped taking imipramine one week previously after an oculist had told him it may be affecting his vision. He had then commenced overdosing with meprobramate (20 tablets of 400 mg. per day). Imipramine therapy was recommenced, and he has remained symptom-free on one tablet three times a day.

The commonest side effect was sweating (nine cases), which generally did not appear to disturb the patient.

Generalized pruritus without rash was complained of in three cases.

Bizarre nocturnal visual hallucinations in one case were relieved by withdrawal of the drug.

Three patients complained of nausea and dyspepsia.

There was one complaint of blurred vision and one instance of postural hypotension.

One patient became hypomanic.

Although numerous, side effects were generally well tolerated, and appeared to be directly related to dosage.

Summary.

Imipramine was used in the treatment of 35 adult male patients presenting with depressive symptoms: 11 showed marked improvement, 12 showed moderate improvement and 12 showed slight improvement or no change.

It is suggested that imipramine is a useful addition to the chemotherapy of depression.

Acknowledgements.

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Reports of Cases.

ACUTE INTESTINAL OBSTRUCTION FOLLOWING A VENTRISUSPENSION OPERATION.

By W. STERN, M.B., F.R.C.S.,
Melbourne.

OPERATIONS for the correction of retroverted uteri are now rare, but were common and fashionable as recently as ten to twenty years ago. There must therefore be many women living on whom these operations have been performed. While great ingenuity was expended in devising different methods and techniques, they mainly fell into two groups: (i) the Gilliam types of ventrisuspension and occasionally ventrifixation; (ii) the Baldy-Webster type of ventrisuspension.

The basis of the Baldy-Webster operation is that a hole is made through the avascular area of the broad ligament just to the side of the uterus, and the round ligament is drawn through this hole and sutured together behind and onto the uterus. The broad ligament defect is rarely sewn up again. When this operation was common, its complications were known; but because of its infrequent performance nowadays, a whole generation of surgeons and doctors has grown up unfamiliar with it, though it is mentioned by Ian Aird (1957) as a possible cause of obstruction of the internal hernia type.

As the following case will show, loop obstruction of the intestine must be considered in the differential diagnosis of twisted ovarian cyst in those women who have had the Baldy-Webster operation.

Clinical Record.

Mrs. A., aged 42 years, was referred to me by Dr. B. A. Minto on April 9, 1960, with the diagnosis of acute small-bowel obstruction. Nine hours previously, after having her bowels open, she experienced a sudden severe pain low down in the left iliac fossa and vomited shortly afterwards. The pain became colicky and, after four hours, constant. She vomited again, on one further occasion, five hours after the pain began. No flatus had been passed since the onset of the pain. Her menstrual periods had been regular. A Baldy-Webster operation had been performed elsewhere 14 years previously.

On examination of the patient, her temperature was 97·4° F., her pulse rate 80 per minute, and her respiratory rate 20 per minute. The abdomen was not distended, but there was on palpation marked tenderness low down in the left iliac fossa with pronounced rebound tenderness. On auscultation, excessive bowel sounds and borborygmi were heard. All hernial orifices were normal. Rectal

examination elicited tenderness high up and to the left of the cervix, while bimanual vaginal examination showed a very tender cystic mass palpable to the left of and separate from the uterus. Examination of the chest and heart revealed no abnormality.

A clinical diagnosis of a twisted left ovarian cyst was made. Acute intestinal obstruction was considered in the differential diagnosis. A plain X-ray film of the abdomen was not taken. (The phrase "twisted ovarian cyst" included torsion of a cyst or of a distended Fallopian tube.)

Immediate laparotomy was decided upon. This revealed a strangulated closed loop of the terminal portion of the ileum, which had herniated through the left broad ligament to the side of the uterus from behind forwards, and was tightly constricted by a band containing the left Fallopian tube, the round ligament, the ovary and the ovarian vessels. This was divided, but because of non-viability the strangulated loop was resected and an end-to-end anastomosis performed. The patient made an uninterrupted recovery.

Discussion.

That herniation of gut through the broad ligament defect is possible is obvious when the details of the operation are considered. Congenital defects also occur, but are rare. Small intestinal obstruction following ventrisuspension operations has been recognized for a long time, but its incidence is difficult to determine. Gleadell (1945) found it to be more common after the Gilliam type of procedure, but only because this was more commonly performed than the Baldy-Webster operation.

Goode and Newbern (1944) stated that to their knowledge no case of obstruction and/or strangulation occurring through the broad ligament had been correctly diagnosed before operation; nor was this so in the present case.

The pre-operative diagnosis was wrong, for the following reasons: (i) The distinctive sign of strangulation in the presence of mechanical bowel obstruction — rebound tenderness — is present also when an ovarian cyst "twists" on its pedicle — that is, becomes strangulated. (ii) Passage of flatus is not uncommonly absent. This state of affairs lasts for some hours in the presence of an acutely painful lesion in the pelvis, and may therefore be unhelpful in the early case. Severe pain by itself may induce reflex inhibition of bowel activity — a silent abdomen. (iii) The distant site of the obstruction and the short time interval between onset and referral precluded the appearance of the other signs of obstruction (abdominal distension and persistent vomiting). Ideally, of course, obstruction should be diagnosed before these signs make their appearance. (iv) A plain X-ray film of the abdomen would have confirmed the original diagnosis by showing fluid levels in the obstructed loop, but not necessarily elsewhere — again because the obstruction was of short duration. (v) Ovarian cysts are commonly, but not invariably, associated with menstrual irregularities.

The lessons to be learnt are as follows.

1. Because ventrisuspension operations are rare today, internal hernia as a complication tends to be forgotten. Goode and Newbern (1944) collected from the literature 27 cases of protrusion and/or strangulation of loops of bowel through defects in the broad ligament, and nine of these (one-third) were associated with a previous Baldy-Webster operation.

2. As herniation occurs through the broad ligament, the physical signs of a strangulated loop can be the same as those of a twisted ovarian cyst, as in this case. Commonly twisted ovarian cysts are considered to be less urgent than strangulations, and these patients may therefore be left for some hours before operation is undertaken. Since viability of strangulated gut is related to the period of strangulation, operation for its relief becomes urgent.

3. Acute intestinal obstruction should be considered in the differential diagnosis of twisted ovarian cyst in women who have had a Baldy-Webster operation.

4. Laparotomy should be performed as soon as practicable, and by those willing to proceed to a bowel resection if this should be necessary.

Summary.

A case of acute intestinal obstruction following a ventrisuspension operation is recorded in which the physical signs mimicked a twisted ovarian cyst. The diagnosis is discussed.

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Reviews.

Homosexuality. By D. J. West; 1960. Mitcham, Victoria: Penguin Books. 7¼" × 4¼", pp. 200. Price: 5s. 6d.

DR. D. J. WEST is to be congratulated on his Pelican book on homosexuality. It deals primarily with the male variety, since this produces more social problems than that of the female. The work falls into two sections; the first concerns basic facts and the second causation and treatment.

The author rightly introduces us to homosexuality through a survey of its incidence in different cultures. We are reminded that in some primitives it is a virtue which induces virility. History shows that homosexuality has occurred in all ages, and regressive morality has never achieved its elimination. Homosexual tendencies are commonly observed in mammals and would seem a "deep-rooted natural urge which finds different expression in different cultures". Hints as to the incidence of homosexuality today are based on police prosecutions, statements by homosexuals and *questionnaires*. In Dr. West's opinion one in 20 of all men are predominantly homosexual. Credit is given to the Kinsey report based on 4000 interviews; it estimates that 4% of American white males are exclusively homosexual, and importantly that over one-third of all males "admitted at least some homosexual experience'.

There is evidence that homosexuals fall into the categories of actives and passives, but the difference is not clear cut. Neither physique nor temperament is characteristic. "The most important trait, certainly the one most noticeable to a psychiatrist, is the pronounced sense of guilt and shame." The author writes feelingly of its end results, and states: "The normal man, restricted as he may be by the routine of family life, has no cause for envy."

The legal problem is complicated by the wide-open door of blackmail. Police vice squads, formed to punish offenders, have employed methods of entrapment which have created criminals out of honest men. Paradoxically, impersonators of vice squads have been able to reap the harvest of blackmail by impersonation. There is a wide variation of the laws against homosexuality in different countries. There is evidence that the problem in Germany, Britain and the United States is highlighted in these countries because of the severity of their laws and the publicity which follows. The author's opinion as to value of imprisonment for homosexual acts is that it is most unsatisfactory and embitters rather than aids. Prison life is a practical demonstration of more homosexuality. On release, the prisoner feels that he is "a scapegoat for behaviour for which thousands of others go unpunished".

The concluding section illustrates the complexity of causation and treatment. Although much is known of the relation of endocrines to the sexual urge, stilbœstrol treatment, like castration, may abolish sexual feelings; it is not invariable, and there are unfortunate side effects. Evidence is quoted incriminating intersexuality as a factor in homosexuality, but the matter is *sub judice*, as is that of heredity.

The psycho-analytical approach is treated at length, and this section makes interesting reading. The Œdipus complex and anal fixation are dealt with. The author handles this difficult subject with insight.

Methods of treatment vary from physical punishment to incarceration, from classical Freudian psychoanalysis to

group therapy and persuasion. Each case must be dealt with on its merits. The first consideration must be decision on whether to aim at conversion or reorientation. It is cruel and useless to attempt to convert the unconvertible. Much can be done in many cases by common-sense advice. As might have been expected, the prevention of homosexuality is bound up with the possibility of a changed social outlook.

This "Pelican" should have a place in every practitioner's library. In suitable cases it would be a satisfactory prescription for an intelligent homosexual who needed a new slant on his feelings of guilt.

Pardon My Sneeze: The Story of Allergy. By Milton Millman, M.D.; 1960.: San Diego, California: Frye & Smith Ltd. 8¾" × 5¼", pp. 230 with illustrations. Price: not stated.

MILTON MILLMAN has written this book mainly for the layman. It is written in an easy journalistic style and makes most interesting and amusing reading. The cartoons in the book, which are cleverly done, are of a satirical type, but do help to enliven the interest of the reader, and show an insight into the type of person who has an allergic constitution.

The book covers in 22 chapters the major diseases caused by allergy as known to the layman. The author's description of the mechanism of asthma in the chapter on nervousness and asthma is the only object of criticism in this otherwise excellent publication. The description states that spasm of the bronchial tubes, which become smaller, makes it difficult for the patient to get air into his lungs; rather, it is the difficulty to get air out of the lungs that is the major problem before over-inflation occurs.

The elimination diets have been covered very fully, and a full list of products which contain specific food, inhalant and contactant allergens is given in complete detail.

This publication, although intended mainly for the allergic patient, can be recommended to all general practitioners and physicians who see allergic subjects, as it contains many helpful hints on diagnosing the particular allergen, and furthermore, on how to take simple precautions to avoid it.

The Clinical Application of Antibiotics: Erythromycin and Other Antibiotics. By M. E. Florey, M.D.; Volume IV; 1960. London, New York and Toronto: Oxford University Press. 9¾" × 6", pp. 312. Price: 121s. (Australian).

THIS final volume in the series deals at length with erythromycin, polymyxin and neomycin, and shorter accounts are given of a further 22 antibiotics including spiramycin, oleandomycin, novobiocin, vancomycin and ristocetin. The amphotericins are mentioned, and it is heartening to note that there is now some hope in the treatment of meningitis due to the *Cryptococcus* (torulosis).

There are a series of contradictory statements on the effect of actinomycin in the therapy of malignant conditions, and judgement about its place in the treatment of neoplastic disease must, for the present, be withheld.

In the final chapter, which comprises about one-third of the total text, is a great fund of knowledge, well summarized under the title "The Choice of an Antibiotic" with general considerations. The fallacies connected with sensitivity tests should be well known by now and are clearly stated, as also is the current knowledge on the development of resistance by staphylococci in hospital environments. This chapter includes the indications for all the antibiotics mentioned in the earlier three volumes, and adds a section on the adjuvant effect of special agents such as the corticosteroids and gamma globulin.

Lady Florey has emphasized the dangers of antibiotics and at the same time explicitly pointed out the wide range of effective uses of antibiotics in routine clinical practice.

Medical Care of the Adolescent. By J. Roswell Gallagher, M.D., and the Staff Physicians of the Adolescent Unit; 1960. New York: Appleton-Century-Crofts, Inc. 9¼" × 6", pp. 394, with illustrations. Price: $10.00.

THIS book epitomizes the principal author's extensive experience in the care of young people; his purposes are to discuss those ailments which are common in adolescence, or which present some peculiarity during that period, and to emphasize the importance of understanding and treating people and not just their symptoms. He abjures the promotion of a new specialty, and makes instead a plea for comprehensive "generalist" care; the latter concept forms, indeed, the chief theme of the book.

The introductory chapters contain basic comments on the nature and needs of the adolescent, and the factors which influence the course, evaluation and management of various conditions. A careful outline of the optimal conditions for history-taking and physical examination is included, which merits special attention from anyone who seeks to do effective work with young people. The chapters on growth and development provide a compendium of useful data not otherwise readily available, including Greulich's classification of sexual maturation in boys, Tanner's standards of development in girls and Bayley's tables for estimating growth potential

Diabetes, epilepsy, heart disease and other conditions are discussed with regard to their special implications for adolescents; there are excellent chapters on gynæcological problems; and more specifically adolescent disorders such as acne, fitness and fatigue, visual and orthopædic disturbances and athletic injuries, receive careful consideration. There is little mention of acute conditions such as appendicitis or infectious illnesses, since these usually receive prompt and adequate care. Chronic complaints tend to require the approach which Dr. Gallagher advocates, and in discussing such contentious issues as obesity, enuresis, ulcerative colitis and undescended testicle, he demonstrates with convincing sincerity the dictum that adolescents "need the close relationship and the consistent care which one physician can provide" in the face of confusion and disagreement between other responsible adults.

The final chapters deal with scholastic failure, emotional and adjustment problems and some normal behavioural manifestations concerning sex, rebellion and anxiety. The physician is reminded once again of the significant role he may assume for the disturbed adolescent; and indeed, the book is informed with understanding of the basic concepts of modern psychiatry and its application in general medical care.

The style is clear and direct, though occasionally repetitious. The format its pleasant, but more distinct subheadings would be helpful in some chapters. We should like to have seen some comments on the management of the adolescent in hospital, and upon the physician's relationship with the adolescent's parents. No mention is made of nocturnal emissions or urethritis, surely important items in adolescence, and we hope that future editions may include discussion of stuttering, allergy, asthma and migraine.

This book will be found interesting and useful to anyone concerned with young people and really interested in their welfare.

Industrial Pulmonary Diseases: A Symposium held at The Postgraduate Medical School of London 18th-20th September, 1957 and 25th-27th March, 1958. Edited by E. J. King, M.A., D.Sc., F.R.I.C., and C. M. Fletcher, C.B.E., M.D. (Cantab.), F.R.C.P.; 1960. London: J. & A. Churchill Ltd. 8¾" × 5¾", pp. 284 with 98 illustrations. Price: 32s. net (English).

THIS excellent book, written by acknowledged experts, should be in the possession of all radiologists and physicians likely to be concerned with industrial lung disease. Both groups will be able to see their own disciplines in proper perspective in relation to recent studies of symptomatology and pulmonary function in large populations of miners and other occupational groups. There is also a more than adequate survey of pathology, pathogenesis and, in general terms, prevention; the only less clinical aspect which might also have been considered is the assessment of dust hazards in industry. The several chapters dealing with radiological, functional and epidemiological aspects of most of the pneumonoconioses are excellent and summarize all the important advances of the last decade. Most attention is given to pulmonary conditions, including bronchitis and emphysema, associated with coal and silica hazards; but there is an outstanding exposition of the effects of iron and other radio-opaque dusts by A. I. G. McLaughlin, and other hazards such as talc, asbestos, cotton and radioactive dusts receive attention. The chapter on management contains much that is sound. That it does not fulfil the promise held out by another phrase in the chapter heading—"Natural History"—merely indicates that there is still much to be done before an accurate prognosis can be given in the individual case and before finality can be reached on the question of change of occupation. One cannot agree—there is little in this book to disagree with—that the combination of penicillin and streptomycin should be used for episodes of bronchopulmonary infection in patients with

pneumonoconiosis, unless and until active coexistent tuberculosis has been unequivocally excluded. The difficulty of this in many instances, and the delay involved, indicate that a broad-spectrum antibiotic should be given initially.

It is of some interest to place together several observations scattered through the book; they are considerably simplified for this purpose. Firstly, dust deposition is less in bronchitic lungs than in lungs without bronchitis (Gough and Hepplestón); secondly, bronchitis is commoner in coal-miners than in non-miners, and commoner in miners without simple pneumonoconiosis than in those with it (Higgins and Ball); thirdly, ventilatory capacity is lower in coal-miners without simple pneumonoconiosis than in those with some degree of it (Higgins); fourthly, the standardized mortality rates for categories 2 and 3 simple pneumonoconiosis, which are about the same as for non-miners, are less than for those either without pneumonoconiosis or with category 1 (Cochrane). Surely differences between "no pneumonoconiosis" and "some pneumonoconiosis" are more likely to reflect the effect of chronic bronchitis in the former group than that of supermen in the latter. It seems to be about time that chronic bronchitis was accepted more readily as an occupational disease, even though some subjects would have contracted it anyway.

Symposia these days are being published with too little provocation; but this one fulfils an admirable purpose in presenting the results of research in a variety of specialized fields in a way which stimulates thought and permits easy integration with clinical practice and experience. The only violently adverse reaction which it provokes it shares unfortunately with almost all recent British publications: must the infuriating practice of omitting the titles of references—without even the excuse of space offered by weekly journals—become accepted procedure? In other respects the book is well produced and illustrated.

Cosmetic Surgery: Principles and Practice. By Samuel Fomon, M.D.; 1960. Philadelphia and Montreal: J. B. Lippincott Company. 10" x 6¼", pp. 672, with 608 illustrations. Price: £15 2s. 6d.

IT is unfortunate that the word "cosmetic" is used in the title of this book, thereby perpetuating an erroneous impression that has recently become popular in the lay Press, to the detriment of a bona-fide branch of surgery. "Cosmetic" is derived from the Greek κοσμητικός, skilled in adorning, and is defined by the Oxford Dictionary as "having the power to beautify (the complexion)" and as "a preparation for beautifying the hair, skin or complexion"—meanings which cannot rightly be applied to the specialty of plastic surgery. It is significant that on the title page, the list of appointments held by the author contains the word "plastic" five times, but "cosmetic" not at all.

In this country this word is not generally used by plastic surgeons who are fully qualified to undertake all aspects of reconstructive surgery, but, if used at all, is restricted to those operations designed "to alter contour solely for the purpose of improving the appearance". It was to these operations that we expected to find the text confined, and, in fact, this was promised in the preface.

However, this book of 642 pages is divided into two sections. The first, of 234 pages (more than one-third of the text), is devoted to those general principles of wound closure, tissue handling, transplantation and the like which we endeavour to teach our juniors at an early stage in their training. This is good solid stuff, but much of it is out of place in a book which appears to have been written to interest those in training, or in practice, in plastic surgery. For instance, there are a longish section on diagnosis and treatment of head injuries and many pages on the insertion of sutures and tying of knots—including nearly a page on the origin, preparation and sterilization of catgut.

The second section is of much more interest to the plastic surgeon, and here the chapters on the nose, ear, eye, face and breast are presented in lucid detail and with a wealth of photographs and line drawings. Not everyone will agree with many of the ideas expressed, but we found this section stimulating and of great interest. Some criticisms are typified by Figure 407, which shows, diagrammatically, serial excision of a lesion on the front of the neck with a resultant vertical scar extending from chin to sternal notch. The section on angioma contains many alternative treatments, a number of which are outmoded and out of place in a serious work on surgery.

In summary, it is difficult to know to which class of reader this book could be recommended. It is easy, and true, to say that there is something of interest in it for all, but the amount of interest may be very small in relation to the whole. It should undoubtedly be on the shelves of all libraries as a most useful reference book, but general practitioners looking for something on wound management (as suggested in the preface) would find this an expensive way of obtaining the information.

Pathogenesis and Treatment of Occlusive Arterial Disease: The Proceedings of a Conference held in London at the Royal College of Physicians of London 13th-14th November 1959. Edited by Lawson McDonald; 1960. London: Pitman Medical Publishing Co. Ltd. 9" x 6", pp. 252. Price: 39s. 6d. (English).

THIS book is an account of the proceedings of a conference on occlusive arterial disease held at the Royal College of Physicians of London in November, 1959. It is divided into four sections dealing with pathogenesis of occlusive arterial disease, cerebral vascular disease, coronary artery disease and peripheral vascular disease.

In addition to the four chairmen there were 25 contributors of papers. The whole proceedings, including discussion on papers, apparently verbatim, are included in a small book of some 230 pages. The production of this volume of proceedings is somewhat inelegant, with small typescript and lines of irregular length, tiring to the eyes at night. The contributions are short and pithy. It is, of course, not possible to give a comprehensive account of the four large territories comprising the sub-sections of this book, each in itself worthy of a whole conference. However, the reader is given an up-to-date account by acknowledged experts of modern views of those aspects of these problems on which attention has been most focused of recent years. The coverage is wide, varying from such apparently academic exercises as the formation of artificial thrombi *in vitro* to the management of the ischæmic limb. Naturally, in a book of this nature, all statements and opinions will not meet with full acceptance; for example, we were rather surprised to find that no mention of sympathectomy was made by one speaker when discussing the management of ischæmic rest pain (page 214)—a treatment found to be of great value.

The general impression is given that, although there have been some notable advances in the understanding and treatment of occlusive arterial disease, much remains obscure, and that the treatment of the individual patient in any of the three categories discussed is still far from satisfactory.

This book can be recommended as giving a concise account of fact and opinion concerning recent work on occlusive arterial disease and the problems awaiting solution.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Outline of Fractures including Joint Injuries", by John Crawford Adams, M.D., F.R.C.S.; third edition; 1960. Edinburgh and London: E. & S. Livingstone Ltd. 8¼" x 5¼", pp. 276, with illustrations. Price: 27s. 6d.

"Wolff's Diseases of the Eye", revised by Redmond J. H. Smith, D.O., M.S., F.R.C.S.; fifth edition; 1960. London: Cassell and Company Ltd. 10" x 7¼", pp. 236, with many illustrations. Price: 62s.

"The Pocket Prescriber and Guide to Prescription Writing", by Alistair G. Cruikshank, F.R.C.P.E.; seventeenth edition; 1960. Edinburgh, London: E. & S. Livingstone Ltd. 4" x 2¾", pp. 316. Price: 6s.

"Clinical Pharmacology", by D. R. Laurence, M.D., M.R.C.P., and R. Moulton, M.B.; 1960. London: J. & A. Churchill Ltd. 8" x 5¼", pp. 498. Price: 32s.

"Gynecological Urology", compiled and edited by Abdel Fattah Youssef, M.B., D.S., D.G.O., M.Ch., F.I.C.S.; 1960. Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications Ltd. 9" x 5¾", pp. 910, with many illustrations. Price: £9.

"V Congreso Venezolano de Cirugia", volume II; 1959. Caracas: Sociedad Venezolana de Cirugia. 9" x 6½", pp. 572, with many illustrations. Price not stated.

"Expert Committee on Rabies: Fourth Report", World Health Organization Technical Report Series, No. 201; 1960. Geneva: World Health Organization. 9¼" x 6¼", pp. 28. Price: 1s. 9d.

The Medical Journal of Australia

SATURDAY, DECEMBER 3, 1960.

MEMBERSHIP EXAMINATIONS FOR PHYSICIANS' COLLEGES.

IT is gratifying to learn that a reciprocal arrangement has now been effected between the Royal College of Physicians of London and The Royal Australasian College of Physicians in relation to examinations for Membership. The effect of this is that Members of the Australasian College who wish to take the Membership of the London College and likewise Members of the London College who wish to take the Membership of the Australasian College, may, if they wish, apply to the College concerned for exemption from the written papers for the examination. Each case will be considered separately by the Censors' Board, who will take into account the candidate's age and experience; if the application is approved, the candidate will be required to take only the clinical and oral parts of the examination.

This arrangement is the result of discussions that have been going on for some little time. The matter was considered by a committee appointed by the London College in 1958, whose report was issued in April of this year. In this report the committee referred to the increasing number of doctors visiting the United Kingdom to undertake research and post-graduate clinical training, but pointed out that those with the Australasian Membership were often in doubt whether to sit for the examination for the London Membership, the respective Memberships being regarded by many in Australasia as comparable. The committee quoted figures over the past twenty years to indicate that the number of candidates from Australia and New Zealand was not in fact decreasing, despite suggestions to the contrary, but agreed that it would be to the advantage of both Colleges if a degree of reciprocity could be attained. The Australasian Membership examination was regarded as being of a very high standard, and little difficulty seems to have been experienced by the committee in making a recommendation for exemption from the written examinations for those who hold the Australasian Membership and whose application is approved by the Censors' Board. In due course the College accepted the recommendation. It is provided, reasonably enough, that candidates who have been unsuccessful in the examinations must reapply for exemption at each subsequent attempt. A further provision is that the arrangement should be subject to revision in the event of an alteration in form or standard of either the Membership examination of London or the Australasian Membership examination; this is particularly pointed by the firm adherence of the College to the principle that the Membership examination should be an examination in general medicine and that there should not be any concessions on grounds of specialization.

The decision of the London College was earlier this year conveyed to the Australasian College, which in its turn determined to make similar concessions to Members of the London College desirous of taking the Australasian Membership. Appropriate alterations have been made to regulations and by-laws, and the reciprocal arrangement is now in effect. It is a pleasing token of mutual confidence between the two Colleges, which should serve to bind them closer together. More important, however, from the practical point of view is the fact that Australians and New Zealanders in England who are Members of the Australasian College, and who wish to take the London Membership, will not have to divert to studying for the written paper time and energy that they can use much more profitably in gaining experience in institutes and departments in which they are working. Such experience is always of much more value than the picking up of another diploma by those who go overseas, and the new arrangement is particularly to be commended because it helps considerably towards the establishment of this principle.

COMMENTS ON MEDICAL RESEARCH IN AUSTRALIA AND NEW ZEALAND.

THE Life Insurance Medical Research Fund of Australia and New Zealand has, since 1953, made annual grants totalling £270,000 in support of research into cardio-vascular function and disease. It has provided six travelling fellowships, four research fellowships in Australia and 67 grants-in-aid of research programmes. A review of this experience by those concerned with the administration of the fund has given rise to some general comments concerning the conduct of cardio-vascular research, and as these are also pertinent to medical research in general in this part of the world, it may be of value to pass them on.

The important ingredients of research are the research worker, the project and the environment in which the work is done. It is suggested that most success is achieved by putting the accent on the individual as the vital centre of research, and the best research work is done where the investigator responsible for the project is an active participant and has a strong personal conviction that a solution exists. Enthusiastic pursuit diminishes the more aloof the investigator places himself from the work. It is therefore regrettable that there is a tendency to allocate too much of the practical aspect of research to trained technicians. In relation to the second ingredient, best results are produced when there is a clearly defined single project. All work inevitably becomes more involved as it proceeds, thus creating the dangers of dispersion and digression, and a judicious elasticity must be allowed. There is, however, a tendency for many investigators to attempt too much.

The third ingredient, the environment for research, is important, and in this respect it is significant that cardiovascular research with few exceptions is concentrated in university departments, while there is a tragic deficiency of research of all types in university teaching hospitals. Full-time units in hospitals are increasing in number and making their contribution, but all too often they are the subject of professional suspicion and scientific criticism. Before applied research can develop to its proper extent, it would seem that certain basic changes are necessary. One is that the governing bodies of hospitals should be sympathetic to teaching and research responsibilities. This would be aided by the liberation of the teaching hospitals from predominant regional governmental control. Secondly, close cooperation should be encouraged between universities and teaching hospitals as regards physical and clinical facilities and intellectual intercourse. Physical proximity of the two institutions is an enormous advantage. Thirdly, members of the visiting and full-time staff of hospitals should have comparable status, and this could be achieved through university appointments.

The keystone of worthwhile research is the research worker. In addition to material aids, he needs financial security, mental leisure and a healthy environment for his activities. These conditions are in general lacking in our hospitals. Consequently there is a constant loss of enthusiastic and able young men who could be making a contribution in the field of research and, incidentally, improving the standard of their hospital.

Current Comment.

NEW HORIZONS IN DIABETES.

THE prevention of diabetes mellitus, were it to become possible, would make necessary an entire rethinking of the problem of diabetes and would force on us a new concept of acceptable standards of care for patients who were potentially diabetics. Two relevant questions then are: (i) Can the onset of diabetes mellitus be accurately predicted? (ii) Can its onset be avoided? The answer to both questions is probably in the affirmative.

That diabetes tends to run in families has long been known. Frezal from Leyden and other workers have reported the investigation of a series of 500 diabetics.[1] Of the relatives 6·6% were found to be diabetic too. In siblings the incidence of diabetes was 3·1%. Consanguineous marriages or marriages in which diabetes was to be found on both sides showed an increased incidence of sibling diabetes. It is suggested that a single gene causes a heterozygotic and mild form of diabetes, whereas the double gene produces homozygotic and severe forms. These workers consider that all the usual causes only act to uncover a previous inherent liability to diabetes.

As one contributor to a valuable symposium on "Diagnosis of Incipient Disease" R. Levine[2] has discussed the pre-diabetic patient. He states that, apart from obesity and early mild abnormalities in the results of glucose tolerance tests, the earliest manifestation of diabetes is a genetic constitution. Conn (of aldosteronism fame) has been working on a cortisone-glucose tolerance test. Steroids cause increased gluconeogenesis, aggravate existing diabetes and may unmask a pre-diabetic subject, revealing altered glucose tolerance. Conn, with a provocative dose of steroids, seeks out these pre-diabetic subjects who have still been able to hide the fact of their beta-cell insufficiency. His test has yielded positive results in 25% of relatives of diabetics, and already some members of the series he has been studying have developed frank diabetes.

We now know the group in which case seeking would be rewarded, and we have a way of finding them. Once they are found, the importance of the control of obesity cannot be overstressed. With all this in mind Professor A. Loubatière's work[3] on orally administered hypoglycæmic agents becomes most important. The sulphonylureas apparently act by liberating more intraprotoplasmic insulin particles. Professor Loubatière does not think that insulinase or its inhibition plays any part in the hypoglycæmic action of the tolbutamide-carbutamide type of drugs. After the prolonged use of these drugs, beta cell regeneration and islet cell hyperplasia have been reported. Loubatière instances young diabetics with an undoubted familial trait whose diabetes is of recent origin and has not yet resulted in weight loss, and in whom treatment with these sulphonamides can cause the diabetic symptoms to disappear at least for a time. The glucose tolerance curve returns to normal in some cases and has remained normal for up to two years.

It seems that the diabetic must be treated before he indeed becomes frankly diabetic. We must come to the aid of his last few surviving beta cells in the pancreas about to go down entirely and irrevocably before a rising tide of hyperglycæmia. Weight reduction and "first aid" to his sore-pressed beta cells by our hypoglycæmic agents may prevent him from getting diabetes. In the future this may become the main and more rewarding place of the hypoglycæmic sulphonylureas in modern therapeutics.

OCULAR CHANGES AFTER HÆMORRHAGE.

THE changes which may occur in the fundus oculi after severe hæmorrhage, particularly from the gastro-intestinal tract, are the subject of a recent review by M. A. Pears and G. W. Pickering.[1] Two types of lesion may occur. The least common is sudden blindness succeeded by optic atrophy. The other type is much less well known because it is symptomless and therefore seldom looked for, but the appearances may be most striking and closely resemble those of hypertensive neuroretinopathy. Both types of lesion were fully described and discussed by W. R. Gowers over half a century ago.[2] Contemporary texts on ophthalmology give little attention to these ocular changes, and gastro-enterological works do not even mention them, the reason perhaps being, as Pears and Pickering wryly remark, that "ophthalmologists are now rarely called to see a patient unless sight is disturbed, and gastro-enterologists rarely carry ophthalmoscopes".

Loss of vision after hæmorrhage is fortunately now rare, perhaps because better methods of resuscitation are available. In the only case of this type seen by Pears and Pickering, vision was permanently lost in one eye after severe melæna. At first no abnormality was noted apart from dilatation of the pupil. The next day the retinal veins were found to be congested. Five days after the onset of blindness venous engorgement was still present, and the disk was observed to be swollen. Four weeks later optic atrophy developed. The mechanism of these changes is not clear. Autopsy reports by Ziegler[3] and Goerlitz[4] of patients who died shortly after they became blind describe changes in the optic nerve which could cause both loss of vision and papilloedema. The major changes observed were immediately behind the lamina cribrosa of the optic nerve, where there were round or oval foci of degeneration of the nerve fibril sheaths, in which there were signs suggesting commencing glial

[1] *Excerpta med. (Amst.), Sect. VI*, June and July, 1960.
[2] *Med. Clin. N. Amer.*, 1960, 44: 203 (January).
[3] *Proc. roy. Soc. Med.*, 1960, 53: 595 (August).
[1] *Quart. J. Med.*, 1960, 24: 153.
[2] "A Manual and Atlas of Ophthalmoscopy", 4th ed., 1904, London: 227.
[3] *Beitr. path. Anat.*, 1887, 2: 361.
[4] *Klin. Mbl. Augenheilk.*, 1920, 64: 763.

hyperplasia. Such changes would be consistent with loss of vision followed by transient papilloedema, but the pathogenesis of these lesions is not at all clear.

Of greater interest, perhaps, is the occurrence of ocular changes which are unaccompanied by any symptoms, and which are transient in nature. Pears and Pickering describe seven such cases, in all of which severe blood loss occurred. In two there were exudates only, in three there were hæmorrhages in addition, and in two there was papilloedema as well. In these last-mentioned two cases the changes were indistinguishable from those occurring in hypertensive neuroretinopathy, except that there were no changes in the retinal arteries. Earlier authors postulated that these changes were due to the anæmia which followed hæmorrhage. Pears and Pickering present evidence making this hypothesis unlikely. A much more probable explanation appears to lie in sudden diminution of the circulating blood volume. Pears and Pickering remark that it would be of importance to know whether similar retinal changes occur in other conditions in which a profound fall in blood pressure occurs without loss of blood. They observed hæmorrhages in the fundus of a patient who was in profound shock after a myocardial infarction. However, this patient had received a nor-adrenaline infusion and anticoagulants, and it is therefore impossible to know whether the ocular changes were related to the therapy or to the hypotensive state. Some years ago Pickering[5] presented evidence to show that the cerebro-spinal pressure is raised in anæmia, but this is almost certainly not the whole explanation of the ocular changes in such patients. It is also possible that focal retinal ischæmia may be responsible, but on the data available no hypothesis put forward is convincing. Further investigation of this important manifestation of hæmorrhage is required, particularly because it so closely resembles the changes occurring in the malignant phase of hypertension.

MELANOMA IN PREGNANCY.

IT has long been believed that pregnancy has a deleterious effect upon pigmented nævi. George Pack,[1] who is well known for his writings upon the subject of melanoma, stated at the Conference on the Biology of Normal and Atypical Pigment Cell Growth, held by the Section of Biology of The New York Academy of Sciences in 1946, that he had never seen a patient who developed malignant melanoma during pregnancy survive for any length of time. He went on further to say that any example of malignant melanoma he had encountered which developed during or shortly after pregnancy "grew with startling rapidity and was usually widely disseminated without control by surgical excision, however radical, or by any other method of treatment".

Later, in 1951, Pack and Scharnagel[2] analysed a small series of 32 cases in which melanoma developed just before, during or shortly after pregnancy. They reached the conclusion that pregnancy did augment the malignancy of melanoma, and that this malign influence persisted for a variable length of time after pregnancy. It was pointed out at that time that termination of pregnancy had no influence upon the behaviour of the malignant mole. However, the series was small, and the conclusions were not warranted by the data.

It is well known that pregnancy is associated with increased skin pigmentation, and that moles may darken with pregnancy, but until recently there has been no adequate statistical study to support the popular belief that pregnancy affects moles in an adverse way. Phyllis A. George, Joseph G. Fortner and George T. Pack[3] have now had the opportunity to investigate the behaviour of 77 patients in whom pregnancy and melanoma coincided and a further 38 who became pregnant after being treated for melanoma. They compared these with 330 control subjects who were not pregnant. The clinical course of the melanoma in both groups was essentially similar except that the lesions tended to be larger in the pregnancy group and there were more instances of lymph node metastases at the time of definitive treatment. There was, however, no evidence of any increased rapidity of metastatic spread.

The five-year and ten-year survival rates for the 77 patients in whom pregnancy and melanoma coincided were 50% and 42%; in the 38 patients who became pregnant after definitive treatment for melanoma the survival rates were 47% and 39%. The control group was divided into those aged 16 years to 43 years, in whom the survival rates were 50% and 45%, and those aged 44 years or more, amongst whom the survival rates were 43% and 40%. Although these groups are small, the figures suggest that there has perhaps been an unwarranted pessimism concerning the outcome of melanoma in pregnant women.

[5] *Clin. Sci.*, 1934, 1: 397.

[1] In "The Biology of Melanomas", Special Publication of the New York Academy of Sciences, 1948: 52.

[2] *Cancer*, 1951, 4: 324.

[3] *Cancer*, 1960, 13: 854.

SPINAL ANÆSTHESIA.

SPINAL ANÆSTHESIA is a technique which appears to be falling into disuse. There is little doubt that one of the main reasons for its unpopularity is the fear of neurological complications, with the possibility of lawsuits when such complications occur. These sequelæ have been regarded as unpreventible by many, so that it has been suggested by at least one group of authors (F. Kennedy, A. S. Effron and G. Perry[1]) that "from a neurologist's point of view spinal anæsthesia should be rigidly reserved for those patients unable to accept a local or general anæsthetic". L. D. Vandam and R. D. Dripps[2] are strongly opposed to this view and believe on the contrary that spinal anæsthesia is one of the safest and most satisfactory of all anæsthetic techniques when properly understood and managed. During the period 1948 to 1951 every person who was given spinal anæsthesia at the Hospital of the University of Pennsylvania was studied according to a prearranged plan. A total of 8460 patients, given 10,098 injections of spinal anæsthetic, was available for study. Accurate information was obtained for 89% of the total number of injections of anæsthetics for periods ranging from six months to ten years. No instances of adhesive arachnitis, transverse myelitis or the cauda equina syndrome were found. Minor neurological deficits were noted, but none were progressive or of any consequence.

Analysis of the cases in which minor neurological deficits occurred revealed that the patients could be divided into two groups—one in which there had been antecedent neurological disease and the other in which there had been no previous history of such disease. Since 11 patients were found who showed exacerbation of neurological disease after spinal anæsthesia, it is advised that spinal anæsthetics should not be given to a patient with disease of the nervous system. In the second group, comprising 17 patients, it was considered that the symptoms and signs were due to traumatic lumbar puncture rather than to the actual injection of spinal anæsthetic solutions. Such effects then should be preventible by the careful selection of patients; the patient with marked obesity, spinal curvature or arthritis should be excluded from spinal anæsthesia. Attention to details of technique in the performance of lumbar puncture was emphasized.

Vandam and Dripps have made out a strong case for the use of spinal anæsthesia, and there seems to be little doubt of the safety of the method in their hands. However, in view of the extremely satisfactory results now possible with general anæsthesia, it seems unlikely that any other technique—whether spinal anæsthesia, local anæsthesia or hypnotism—will be widely used in the present era.

[1] *Surg. Gynec. Obstet.*, 1950, 91: 385 (October).

[2] *J. Amer. med. Ass.*, 1960, 172: 1483 (April 2).

Abstracts from Medical Literature.

SURGERY.

Cancer of the Colon and Rectum in Young Persons.

J. W. JOHNSON, E. S. JUDD AND D. C. DAHLIN (*A.M.A. Arch. Surg.*, September, 1959) review a series of 222 histologically proved malignant neoplasms of the colon and rectum in persons aged 16 to 29 years, which have been encountered in a 30-year period at the Mayo Clinic. Of these 169 were cases of adenocarcinoma without associated ulcerative colitis or multiple polyposis. The authors analysed the clinical features of the 95 cases of adenocarcinoma in which resection was performed, and found no features which were different from those of older groups, although they thought that pain was a more predominant symptom. The location of the lesions in the colon seemed about the same as in older patients, except that the rectum was involved less frequently in the younger group. The incidence of higher grade lesions (Broder's classification) and of lymph node involvement (Type C, Dukes's classification) was distinctly higher in the youthful patients than in older ones. The surgical mortality rate was lower for younger patients. The authors describe two lesions which were considered inoperable because of local fixation, and which were subjected to radiation therapy. One patient was alive 18 years, and another 20 years after this treatment. Of the 95 patients on whom resection was performed, 20 are still living from 10 to 29 years later.

Intestinal Lipomatosis.

C. S. LING, C. LEAGUS AND L. H. STAHLGREN (*Surgery*, December, 1959) report a case of intestinal lipomatosis which, they state, is a very rare condition. There may be no signs or symptoms of lipomas of the intestines, and many of these lipomas are found only at autopsy. Symptomatic lipomas usually arise in the submucosa and project into the lumen of the bowel. Symptoms are usually due to intussusception caused by these tumours. Bleeding due to ulceration of the mucosa overlying a tumour is less common. Lipomas of the colon produce symptoms twice as frequently as lipomas of the small intestines. On barium X-ray examination submucosal lipomas produce filling defects, and when multiple lesions are present a "soap bubble" appearance is seen. It is pointed out that lipomas may also be more radiotranslucent than the surrounding tissues, and owing to their compressibility change their shape during the examination when external pressure is applied. The operative procedure necessary in such patients is designed to relieve obstruction or bleeding. Care must be taken to conserve as much of the intestine as possible, and only the larger lipomas should be "shelled out" through multiple serial enterotomies. Sometimes a limited resection of the segment of intestine is necessary where the greatest concentration of lipomas is found. The authors consider that prognosis is good, although recurrent intussusception or gastro-intestinal bleeding may occur. They do not consider that the incidence is familial.

Acute Epiploic Appendagitis.

T. C. CASE (*Surgery*, December, 1959) states that epiploic appendagitis should no longer be considered a surgical or pathological rarity, and reports four cases of this disease. He states that acute abdominal pain, with or without an associated palpable mass, is the most significant symptom produced by an acute epiploic appendagitis. If the pain is on the right side, acute appendicitis is the usual pre-operative diagnosis, whereas on the left side sigmoid diverticulitis is the diagnosis. Three-quarters of the cases reported in the literature of epiploic appendagitis occurred in either the caecum or sigmoid colon, the remainder being distributed throughout the rest of the colon, excluding the rectum. The author considers that pre-operative distinction between acute epiploic appendagitis and acute appendicitis can only be speculative, but he points out that the condition should be entertained in the differential diagnosis in cases of right or left lower quadrant pain if nausea and vomiting are not present. The treatment is surgical, in order to avoid the possible complications of an acute progressive disease process.

Ambenonium Chloride in the Prevention of Post-Operative Ileus.

C. BILVAO *et alii* (*Surgery*, December, 1959) have treated prophylactically 400 surgical patients with ambenonium chloride to prevent the development of abdominal distension, the dose being in the majority of cases 1 ml. of an aqueous solution of one part of ambenonium chloride in 16,000, given every four hours after operation. The authors state that in 398 of the 400 cases abdominal distension was prevented. Statistical comparison with a control group shows a significant difference, χ^2 being equal to 17. There were very few reactions after more than 7800 injections, only 0·14% of which were followed by a toxic reaction. Treatment had to be discontinued for one patient as the injection initiated an attack of asthma. The authors state that it is their clinical impression based on this series that prophylactic treatment with ambenonium chloride was more effective than neostigmine administered in a similar manner.

The Sudomotor Test.

R. L. CROSS, M. E. DODDS AND E. M. KNIGHTS (*Surgery*, December, 1959) report the use of a sudomotor test in which a filter paper impregnated with silver chromate is moistened with chloride-free water, and the chloride contained in sweat provides a handprint. This test is devised to outline areas of decreased perspiration in the cutaneous distribution of lacerated or injured nerves. It has been used for evaluation and clinical follow-up in cases of peripheral nerve injuries and is based on the absence of perspiration from sweat glands in the distribution of lacerated peripheral nerves. The authors state that regenerating nerves show a concomitant recovery of the sweat pattern in the areas of their distribution and that the sudomotor test is therefore a valuable prognostic procedure. They suggest that it could prove useful in detecting psychoneurotics and malingerers. They consider it to be of considerable value in the evaluation of nerve injuries, when a decision is required as to the necessity for reoperation and resuturing.

Survival Rates in Gastric Cancer.

R. F. RUSH *et alii* (*Cancer*, May-June, 1960) have attempted to evaluate and compare results of subtotal gastrectomy and of total gastrectomy in the treatment of gastric carcinoma. It was found that not only was the post-operative mortality lower for subtotal gastrectomy, 8·8% against 12·8%, but the five-year survival rate was greater, being 25% against 9%. Furthermore, the survival rate of patients who had total gastrectomy for lesions that could presumably have been treated by partial gastrectomy was 10·5% compared with 25% in patients treated by subtotal gastrectomy. The authors consider that total gastrectomy is not the most suitable choice for routine treatment and should be reserved only for those lesions so large that the whole stomach must be removed for extirpation of the growth. They suggest, too, that the shorter survival rate of patients after total gastrectomy is partly due to the severe nutritional problems which ensue.

Patients with Old Myocardial Infarction.

M. M. WEISS, SR, AND M. M. WEISS, JR (*Surgery*, December, 1959) report a study of 50 patients who underwent 64 major surgical operations four weeks or more after an acute myocardial infarction. There were 47 men and 7 women, ranging in age from 46 to 86 years. There were 6 deaths, all of men, and all died within 48 hours after the operation. Three-fourths of the patients were operated on within 6 years after the myocardial infarction, but one had his episode 12, another 15, and another 22 years before the operation. Six patients had had two myocardial infarctions. The authors consider that their study confirms the experience of other reports that myocardial infarction, after at least 4 weeks of treatment, need not of itself ban major surgery. They conclude that myocardial infarction patients must be meticulously guarded against apprehension and fear, and that hypoxia and marked falls in blood pressure must be specially avoided.

Neurotoxicity of Angiocardiographic and Aortographic Contrast Media.

E. M. LANCE AND D. A. KILLEN (*Surgery*, December, 1959) state that adverse reactions resulting from clinical applications of the contrast materials currently employed for angiocardiography and aortography are being noted with increasing frequency. Many of the more serious of these complications have been the result of insult of the contrast agents to the central nervous system. The authors therefore undertook an experimental evaluation of the neurotoxicity of the more commonly used angiocardiographic and aortographic contrast media. They used sodium iodide (54·6% solution),

"Urokon" (70%), "Neo-Iopax" (75%), "Miokon" (90%), "Diodrast" (70%), "Hypaque" (90%) and "Thorotrast" (25%) on unselected adult mongrel dogs under anæsthesia; the abdominal aorta was exposed by laparotomy and the test solutions were injected; the central nervous system was then examined for evidence of neurotoxicity. The authors found that the capability of the currently available angiocardiographic and aortographic contrast media for causing central nervous system injury is founded upon their cytotoxic effect, which is dependent upon their chemical structure. The authors grade the neurotoxic potential of the seven contrast materials in descending order of toxicity as follows: sodium iodine, "Urokon", "Neo-Oopax", "Miokon", "Diodrast", "Hypaque" and "Thorotrast". In this study "Hypaque" and "Thorotrast" exhibited the least affinity for central nervous system tissues. However, "Thorotrast", because of its relatively low radiopacity, propensity for engendering a local granulomatous reaction, and suspected cancerogenic potentiality, is unsuitable for general use. The authors therefore consider that "Hypaque" is the best medium for angiographic visualization.

Adenocarcinoma of the Large Bowel.

V. A. GILBERTSON (*Surgery*, December, 1959) reviews 1340 cases of adenocarcinoma of the large bowel, all of which have been followed up. These patients were seen at the University of Minnesota Hospitals between 1940 and 1955. Two-thirds of the patients with cancer of the colon died of their disease within five years. When the patients underwent excision for cure, about two-thirds of those with colon cancers and one-half of those with rectal cancers survived five years. When patients with Dukes's A lesions were considered, 83% of those with colon lesions survived five years, including all of those with lesions of the splenic flexure, hepatic flexure and transverse colon. Patients with transverse colon lesions (90% five-year postoperative survival) had the most favourable prognosis; those with rectal lesions had the least favourable prognosis, only 49% having survived five years after operation. The author states that the popular reluctance to employ larger operations for large cancers received little support from this series, in which large excisions allowed substantial survival of patients who might otherwise have been inoperable for cure. Curative excisions in the younger age group (44 years or younger) were followed by acceptable survival rates. However, this was not noted in patients aged over 80 years, except in cases of transverse colon lesions. Palliative excisions were associated with measurable palliation, as were colostomies performed without resection. However, caecostomy, catheter enterostomy and ileostomy were not associated with palliation.

Choledocho-Duodenostomy for Stenosis of the Lower Portion of the Common Bile Duct.

F. SCHWARTZ *et alii* (*Surgery*, December, 1959) consider that side-to-side choledocho-duodenostomy is a simple and effective procedure for relieving biliary tract obstruction due to stenosis of the lower end of the common bile duct. They state that this procedure has also been used to prevent formation of recurrent common duct stones secondary to a relative stenosis. They consider that a stoma one inch or more in length is essential as it ensures patency, and allows free drainage of the contents of the biliary tract into the duodenum. They report the cases of 11 patients who have had this operation, and in the follow-up period, ranging from six months to five years, they have found no complications or recurrence of biliary tract disease.

Carcinoma of the Thyroid in Children.

R. HOWARD (*Aust. N.Z. J. Surg.*, May, 1960) states that carcinoma of the thyroid gland in childhood, though not common, is being diagnosed with increasing frequency, and that one of its most interesting facets is the part played by irradiation in its ætiology. The relevant literature is briefly reviewed, and the author refers to three cases treated by himself, in each of which the neck was irradiated during the first year of life. Two of these cases have already been reported, and supplementary information on these is furnished. Details are given of the third case in which irradiation to a total dosage of 2400*r* was given for a cutaneous hæmangioma in the region of the chin, commencing shortly after birth. It is concluded that the relationship of irradiation of the thyroid during the early years of life to the subsequent development of cancer in this gland is a definite one.

Fatal Post-Operative Pancreatitis.

E. S. R. HUGHES AND G. A. KUNE (*Aust. N.Z. J. Surg.*, May, 1960) state that fatal pancreatitis occurring after surgical operations has attracted attention in the last few years, and report three such cases. In each case the preceding operation was conducted on the biliary tract. In one, the operation was confined to removal of the gall-bladder, but in the other two the common bile duct was explored. In all cases the complication appeared within four days of the operation. At autopsy, the pancreas showed œdema and fat necrosis, but minimal hæmorrhage. Circulatory collapse and upper abdominal pain were the initial symptoms in two patients; in the third the onset was less acute. A second exploratory operation was conducted in two patients, but was not well tolerated. The authors suggest that the complication might be prevented by the surgeon handling the pancreas with great care, by avoidance of unnecessary explorations of the common duct, and by the exercise of extreme care when performing pancreatic biopsy.

Essential Renal Hæmaturia.

J. B. SOMERSET AND G. C. HARKNESS (*Aust. N.Z. J. Surg.*, May, 1960) present a brief review of the history of essential hæmaturia and discuss the condition in the light of the clinical and pathological findings in a series of seven patients submitted to nephrectomy. The gross external appearance of the kidneys in their series was normal, but macroscopic changes were present in the renal pelvis, consisting of petechial or purpuric hæmorrhages in or under the pelvic mucous membrane. Microscopic examination showed dilatations of the small vessels of the renal pelvic submucosa, degenerative changes in the vessel walls with adjacent areas of hæmorrhage in the loose subepithelial connective tissues and evidence of the passage of red cells directly through the pelvic epithelium without apparent break in its continuity. There was evidence to suggest that a process of "healing" occurs. The authors state that the cause of the changes listed is a matter for conjecture, but that their nature suggests that they are the result of some unidentified inflammatory agent. It is suggested that management of such cases should tend towards conservatism, with repeated and prolonged follow-up investigation. However, the authors note that it is not possible to give an absolute assurance that a malignant neoplasm is not present, and express surprise at how much pressure was brought to bear by patients and relatives in favour of nephrectomy for this reason.

Œsophageal Atresia.

R. HOWARD (*Aust. N.Z. J. Surg.*, May, 1960) discusses the management of cases of œsophageal atresia in which the œsophageal deficiency is so great as to render impossible a direct anastomosis between the two segments. Indications are formulated for the use of a visceral transplant in the œsophageal construction necessary in such cases. It is suggested that the colon is the viscus most suitable for this purpose, and that it should be placed intrapleurally along the posterior part of the mediastinum. A case of œsophageal atresia is reported in which a new œsophagus was built using transverse colon as such a transplant.

Carcinoma of the Gall-Bladder.

A. HORWITZ AND J. ROSENSWEIG (*J. Amer. med. Ass.*, May 21, 1960) state that carcinoma of the gall-bladder today ranks sixth among the malignant neoplasms of the digestive tract and causes 6500 deaths annually in the United States. They cite two patients with gall-stones who refused surgical intervention for 9 and 15 years respectively, and eventually died of carcinoma of the gall-bladder. They are concerned by the fact that many authors minimize the danger of cancer of the gall-bladder, and that many of their own patients who developed carcinoma of the gall-bladder had harboured stones for many years, but had been advised against cholecystectomy for "silent" gall-stones. Of 645 patients operated upon for gall-bladder disease by one of the authors, stones were found in 98% of cases, and 20 were found to have carcinoma of the gall-bladder. Nineteen of the latter died within 20 months of operation. All carcinomas occurred in patients over 50 years of age, and gall-stones were present in every case but one. The authors conclude from their figures that of patients with gall-stones, aged 50 or more, 1 in 16 will probably develop carcinoma of the gall-bladder.

The Wider View.

PULMONARY TUBERCULOSIS IN A HONG KONG SANATORIUM FOR REFUGEES.

HONG KONG has an estimated population of about three million people, of whom one million are classed as refugees. The Government of the Colony provided housing for about 400,000 of these, but many of the others are living in crowded conditions in wooden shacks on the hillsides, which are a real menace with regard to fires.

Rennies Mill Camp on Junk Bank has about 10,000 refugees, many of whom were former Nationalist soldiers; some have brought their wives and children out of China to join them. This community is partly self-governing, and for political reasons the Hong Kong Government has not taken any responsibility for it, so it is officially attached to Formosa. Recently the Hong Kong police have established a local police station overlooking the camp.

There is a general medical clinic under the auspices of the Junk Bay Medical Relief Council, and the English woman doctor treats nearly 100 patients daily. Also there is a tuberculosis clinic caring for about 100 patients, half of whom are former inmates of the sanatorium. A small maternity home is kept busy delivering babies daily.

The Hong Kong Medical Department reckons that there are about 60,000 cases of active pulmonary tuberculosis in the Colony, which is 2% of the population. Only about one-tenth of these people are being treated in out-patient clinics, and there are about 1500 in-patient beds. The death rate is falling steadily, but is still 77 per 100,000.

The school-children are tested regularly by the Mantoux test, and 77% give positive results up to the age of 14 years; the proportion rises to 90% in those aged 20 years. Tuberculosis in children mainly affects the mediastinal glands, and there are very few pulmonary complications. About 70% of the new-born babies are inoculated with B.C.G. in the first month.

Five years ago it was decided by the Junk Bay Medical Relief Council to open the Haven of Hope Tuberculosis Sanatorium on the shores of Junk Bay, about half a mile north of Rennies Mill Camp. This has grown from very small beginnings, till now there is space for 180 patients—100 men, 50 women and 30 children. Next year it is planned to build another forty-bed male ward.

Recently the Nansen Tuberculosis Rehabilitation Centre has been opened to take 40 patients with chronic pulmonary tuberculosis, whose sputum, in spite of intensive prolonged treatment, still contains tubercle bacilli. The idea is to isolate these infectious patients from the general community, and to encourage them to look after themselves and also to do a little work to help toward their support and maintenance. It is also planned to build a preventorium, to house 100 children whose parents have active pulmonary tuberculosis.

In October, 1960, a mass radiological survey was made of all Rennies Mill residents, and included villagers and fisher folk in Junk Bay area.

The staff of the sanatorium consists of two resident doctors (English and Australian), a Norwegian matron and an American assistant. There are four fully-trained Chinese nurses, eight graduates of the Sanatorium Tuberculosis Training School, and 40 trainees. The last-mentioned do a two-year training course in the sanatorium, which costs £60 (Australian) for the two-year period. The sanatorium beds are maintained at a cost of £200 (Australian) *per annum* by various church and relief organizations, and the Hong Kong Government pays for 60 free patients. At present four beds are being maintained by gifts from individuals or groups in Australia.

During the period from September 1, 1959, to August 31, 1960, I treated 150 male patients at the Haven of Hope Tuberculosis Sanatorium, Junk Bay, Hong Kong. During this period 54 have been discharged, with sputum free from tubercle bacilli, and with lesions quiescent or completely absorbed in the early cases. There were six successful surgical cases; four patients who had had lobectomies and two who had had thoracoplasties were sent home. Unfortunately, there are two surgical patients with persistent broncho-pleural-cutaneous fistulas, which are discharging much tuberculous pus. Six patients died—three from slowly increasing myocardial failure, one from massive hæmoptysis and two from bronchopneumonia after severe hæmoptysis.

The average period of stay in the hospital for those admitted in 1959 and 1960 was six months. Those admitted before that time had an average stay of two and a half years, and some of these are still inmates, waiting operation or transfer to the Nansen Centre if they become well enough to be up and about.

The ages varied from 15 to 70 years; but two-thirds were between 20 and 40 years, one-fifth between 40 and 50 years, one-tenth between 50 and 60 years, and six over 60 years. The occupations listed were nearly 30, the highest incidence being as follows: factory workers, 16; students, 15; labourers, 15; teachers, 10; farmers, 8; fishermen, 8. The duration of illness before admission to the sanatorium varied considerably. Eighteen patients gave a short history of under six months' illness, and those with early infiltration (15) or bronchopneumonia (3) all did well. The remainder had histories extending from one to over 10 years. About 100 had one to five years' illness, 20 between 5 and 10 years' illness and 12 over 10 years' illness. The universal symptom was cough, with sputum varying from minimal to large amounts of frothy fluid, and about 100 gave a history of hæmoptysis.

Hæmoglobin values, erythrocyte and leucocyte counts, and erythrocyte sedimentation rates were estimated monthly. On their admission to the sanatorium, 84 patients had a hæmoglobin value over 80%, in 58 the value was over 60% and in 8 it was less than 50%. The improvement noted in hæmoglobin value was as follows: 27 improved by 10%, 25 improved by 20%, 5 improved by 30%, 3 improved by 40%. All patients with a hæmoglobin value below 80% on their admission to hospital were given "Fersolate" tablets and with very few exceptions the figure soon rose above 90%.

Of the blood sedimentation rates, 60 were below 10 mm., 60 were between 20 and 60 mm., 20 were between 60 and 80 mm., and 10 were 90 mm. A steady improvement was noted in almost all cases, and the erythrocyte sedimentation rate was found to be a useful check on response in treatment, on prognosis and on deterioration of the patients' condition. The improvement is indicated in 50 cases: in 20 the figure dropped 20 mm., in 20 it dropped between 30 and 50 mm., and in 10 it dropped over 60 mm.

It was difficult to assess what previous treatment had been given, as most patients had attended one or more clinics for irregular periods, so the amount of streptomycin received was used as a criterion of previous treatment. Fifty patients had never received injections, 30 had received less than 100 grammes, 30 had received between 200 and 300 grammes, 10 had received over 300 grammes. In the early acute cases, one gramme of streptomycin was given by injection daily for three months, with INAH tablets (300 milligrammes per day) and PAS (15 ml. of solution three times a day). Those who had received less than 200 grammes of streptomycin were given daily injections for one month, then bi-weekly injections with INAH and PAS as above. Those who had received more than 200 grammes were given INAH and PAS every day. It was difficult to have tests made on all patients for streptomycin sensitivity, and so the amount previously received was taken as a basis.

Sputum tests were done in all cases before admission to hospital was decided on, and very few patients with chronic disease whose sputum did not contain tubercle bacilli were admitted. Regular tests were done each month, and three monthly negative results in succession were taken as a standard for conversion from "positive" to "negative". One hundred patients gave positive results on their admission to hospital, 30 of these were converted to "negative"; but as many of these patients have been recently admitted—that is, under three months—this is not a correct indication of the final conversion rate. Fifty gave negative results on admission, and all continued to do so; there were no re-conversions to "positive" among the 30 just referred to.

All sputum specimens were collected in the early morning, and those patients without sputum had laryngeal swabs taken. The sputum was concentrated in the laboratory and smears were stained; only in rare cases were cultures made.

The radiological appearances were classified as follows: fibrosis, 73; cavities, 30; fibro-cavitary lesions 30; infiltration, 15; cystic changes, 9; atelectases, 8; gross pleural thickening, 4; bronchopneumonia, 3; nodular lesions, 2; post-operative, 8. This classification was based on the predominating feature seen on the X-ray films, and many showed a mixture of the above-mentioned types. Fibrosis included minimal residual lesions to extensive diffuse bilateral involvement. Of the cavities and fibro-cavitary areas (totalling 60 cases), closure of the cavity occurred in 15. If the cavities were limited to one side, the patients were encouraged to lie and sleep on that side. Also, in accordance with Japanese evidence, INAH was given only twice weekly to these patients with cavitary lesions, on the same day as

streptomycin injections. This is meant to keep the broncho-cavitary junction open as long as possible to prevent early closed cavities, which remain evident on X-ray films indefinitely. Nine cavities closed in three months and six in six months. In 15 patients with early infiltration and in three with tuberculous bronchopneumonia, complete absorption occurred in six months. In nine chronic cases, bullous cystic changes developed, some of these as large as two-shilling pieces. This feature seems a sequel of treatment with INAH, which definitely increases fibrosis; this leads to cystic changes. In eight cases of upper lobe atelectasis, only one lobe reexpanded, and most patients had thick-walled cavities. Four had gross pleural thickening, with very poor lung function.

Discussion.

Hong Kong shows a high incidence of tuberculosis as evidenced by 90% of positive reactors to tuberculin skin tests; but only 2% of these develop chronic progressive pulmonary tuberculosis. These figures are similar to those published in Japan, China and Korea.

It will be noted that 90% have chronic disease on their admission to the sanatorium; these can be divided into (*a*) surgical patients, (*b*) "negative sputum" patients and (*c*) "positive sputum" patients.

(*a*) Thoracic surgery is a major problem in Hong Kong, in which there are estimated to be 10,000 patients who could be cured by surgery; but there are only 300 surgical beds and three full-time chest surgeons. We have at present 30 patients awaiting surgery; yet in 12 months only eight have been operated on. The criteria for surgery have been reduced to cases of unilateral disease with cavities and "positive" sputum, after six months' medical in-patient treatment. (*b*) Patients with "negative" sputum are discharged from the sanatorium after three specimens of sputum taken at monthly intervals have been found free of tubercle bacilli. (*c*) Patients with "positive" sputum are transferred to the Nansen Centre if they are able to get about and do light work. The others are kept indefinitely in the chronic ward in the sanatorium.

Summary.

1. Hong Kong's population of 3,000,000 includes 1,000,000 refugees from the mainland of China; 400,000 have been provided with housing by the Government.

2. Rennies Mill Camp on Junk Bay has 10,000 refugees under the jurisdiction of Taiwan. It has a general medical clinic, a maternity home and a tuberculosis clinic.

3. There are 60,000 cases of tuberculosis in the colony, with a death rate of 77 per 100,000. Out-patient clinics treat 6000 patients, and there are 1500 in-patient beds.

4. The number of tuberculin-positive cases rises from 77% at 14 years to 90% at 20 years; 70% of new-born babies are inoculated with B.C.G.

5. The Haven of Hope Tuberculosis Sanatorium on Junk Bay was opened in 1955 and now has 180 patients, a forty-bed male ward being planned for this year.

6. The Nansen Tuberculosis Rehabilitation Centre has been recently opened for 40 chronic patients with "positive" sputum. A preventorium and a mass X-ray survey are additional activities.

7. The sanatorium beds are maintained at £200 (Australian) per year; four beds are now being supported by gifts from Australia.

8. Of 150 male patients treated from September 1, 1959, 54 were discharged from the sanatorium with an average stay of six months and with six deaths. Thirty patients are awaiting surgery.

J. N. BURGESS, D.D.R.,
Haven of Hope Tuberculosis Sanatorium, Hong Kong.

Out of the Past.

THE MELBOURNE HOSPITAL, 1853.

[From the Sixth Annual Report of the Committee of Management of the Melbourne Hospital, 1853.]

OF the [1423] in-door patients, 996 have been cured, 4 discharged, 328 died, and 95 were on the 1st day of January, 1854, remaining in the house. The number of deaths which have occurred, when viewed in relation to the number of persons admitted into the Hospital, might, it is feared if unexplained, excite in the mind of the ordinary observer feelings of dissatisfaction towards those gentlemen under whose care they have been placed. It must be borne in mind that Hospitals in England and elsewhere (except in the case of accidents) are restricted to the reception of curable cases, the incurable and dying being inadmissible. The Melbourne Hospital, on the contrary, receives within its walls persons suffering from disease without reference to the prospect of their recovery. Hence many have been admitted who have breathed their last before the expiration of 24 hours, whilst more than one instance has occurred of the patient dying before removal into the ward. As a forcible illustration, it may be mentioned that out of the 347 persons who died in the house since the first day of January, 1852, 222 were at the time of their admittance either dying, in a hopeless state, or incurable.

With a view to check the practice of bringing persons in a dying state to the Hospital, your Committee brought the matter under the notice of the Coroner, and inquests were held by him in several of the cases referred to, in the hope that by conviction of some of the persons implicated in the removal of the deceased, others might be deterred from similar conduct. The jurors, however, in each case returned a verdict of "Died by the visitation of God". The evil, therefore, remains unchecked, and tends materially to increase the expense for funerals, which amounted during the past year to the enormous sum of £1421, Consequent on the increase in the number of patients, a necessity has arisen for the appointment of additional officers and servants, and the augmentation of salaries and wages. In addition, the Committee have been compelled to provide a permanent bath, a new range for cooking (the one formerly in use being quite inadequate to supply the requirements of the inmates), new water-closets, and a more powerful pump for supplying the latter with water from the well, which in consequence of the insufficient machinery employed had become entirely useless. The dilapidated state of the roof entailed, during the last winter, an expense of £431 1s. 6d. Your Committee by a large expenditure of money and constant attention (having for many months met daily, instead of one day only in each week), have been enabled to maintain the Institution in a tolerable state of efficiency; but they candidly state that from the mischievous practices of many of the patients, and the want of a proper system of drainage, not only must the health of many of the patients suffer, but large and constant expenses be inevitably entailed.

Correspondence.

VITAMIN B_{12} DEFICIENCY IN LEUKÆMIA.

SIR: We read with interest your "Current Comment" concerning "Vitamin B_{12} Deficiency in Leukæmia" (MED. J. AUST., 1960, 2: 788), but wish to contest the statement of your annotator that "a good case exists for the exhibition of vitamin B_{12} and/or folic acid in all anæmic cases of leukæmia and the proliferative disorders of the bone marrow in general".

As stated, macrocytosis quite frequently occurs in certain myeloproliferative disorders, but the pathogenesis of this macrocytosis is essentially unknown. Only very rarely is the macrocytosis due to vitamin B_{12} and/or folic acid deficiency. Such deficiency may be due to coincident pernicious anæmia (there is evidence of such association being more frequent than by chance alone); to gastric atrophy; to small intestinal malabsorption; or to nutritional deficiency. In our experience, long-standing hæmolysis may also occasionally result in mild folic acid deficiency, presumably due to the increased demand.

In such circumstances, where a deficiency of vitamin B_{12} or folic acid can be demonstrated or reasonably suspected, these substances should certainly be given. But there can be no case for the use of "buckshot therapy" of the type advocated, even if subclinical deficiency can be shown to be more common than is generally suspected. It cannot even be claimed that "blind" therapy of this type at least does no harm, since evidence is accumulating to suggest that the administration of folic acid may precipitate a relapse in leukæmia. As long as such possibility exists, there can be no excuse for irrational exhortations of this type.

Unlike your annotator, we have not been impressed by any widespread "ingrained reluctance" to use "buckshot therapy". Multi-compound preparations enjoy wide and ever-increasing sales. A little encouragement of the type offered by your annotation could easily produce the ultimate absurdity of a bright, shiny capsule containing "folic acid" for the anæmia and an anti-folic agent for the leukæmia. Perhaps it would be only thus that the superstitions of polypharmacy could finally be neutralized.

Yours, etc.,

H. LANDER,
H. N. ROBSON.

Department of Medicine,
University of Adelaide.
November 18, 1960.

POSITION OF RADIOLOGIST AT MILDURA BASE HOSPITAL.

SIR: Your issue of November 5, 1960, contains an advertisement for this position. The advertisement contains the statement: "The present appointee has been Radiologist at this Hospital for 9 years, but has decided to accept an appointment in a Melbourne Hospital." It is because the conditions of engagement have been changed to those outlined in the advertisement that I am leaving Mildura.

Yours, etc.,

KARL UHD.

187 Deakin Avenue,
Mildura,
Victoria.
November 7, 1960.

WANTED: AN ANÆSTHETIST FOR VELLORE.

SIR: I am writing to tell you of our urgent need for an anæsthetist. This is a teaching hospital of over seven hundred beds, an affiliated Medical College of the University of Madras, and we do about four hundred operations in the main operating rooms each month. Most of these are major surgery and include intrathoracic procedures of all kinds including open-heart surgery under hypothermia.

At the moment three senior anæsthetists, two American and one British, are working at full speed to cover all the work, but one is leaving unexpectedly at the end of November, after which there will be only two of us to supervise all the juniors and to do as much neuro- and thoracic surgery as possible. This means a serious reduction in the number of cases which can be done each week and will be a very big hardship for many patients. Do you know of any anæsthetist who could drop his work and come and help us soon, even for six months? If you can do anything to make this need known, I shall be grateful. If anyone is interested, will he or she please write to me without delay, giving as many details of experience and the immediate circumstances as possible so as to avoid all unnecessary delay.

Yours, etc.,

GWENDA M. LEWIS,
M.B., B.Ch., F.F.A.R.C.S.,
Professor of Anæsthesiology.

Christian Medical College and Hospital,
Post Box No. 3,
Vellore, S. India.
November 10, 1960.

AMNIOCENTESIS IN HÆMOLYTIC DISEASE OF THE NEW-BORN.

SIR: The article by Dr. Wilfred Cary in your last issue cannot go unchallenged, as it gives false and dangerous impressions of the simplicity and safety of the procedure. In a small series, unsupported by any statistical evidence, no statement, however confident, can be based on firm foundations, and may lead to injudicious use of the method by the inexperienced, and inevitably to its disrepute.

The test is neither as simple nor as safe for mother and baby as the article infers, and the occurrence of heavily blood-stained liquor, and of an unexplained ante-partum hæmorrhage following 12 unsuccessful attempts, are overt admissions of such dangers. Single properly-timed punctures are equally capable of a 95% accuracy in diagnosis and prognosis, as already demonstrated by Walker in 1957, and repeated examinations can only be justified where intra-uterine death is anticipated, or if first examinations produce inconclusive curves.

Dr. Cary admits to an error in diagnosis in 40% of his Rhesus-negative cases, and fails to give criteria for severity of disease or indications for exchange transfusion. The significance of his perinatal loss and the proportion of severe cases in his series are therefore impossible to assess.

The wisdom of advocating wholesale Cæsarean section for purely fœtal indications in already prejudiced infants must be seriously questioned from the obstetric point of view, especially as these babies withstand repeated oxytocic infusions remarkably well.

Finally, no mention was made of the long, tedious spectrophotometric examinations in each case, requiring specialized laboratory facilities. It should be obvious, therefore, that this procedure is far from being routine, either clinically or in the laboratory. Its use at present must still be confined to specialized institutions, and interpretations made only by experienced personnel, if continued benefit to mother and child is to be anticipated.

Yours, etc.,

IAN H. F. SWAIN,
Clinical Superintendent.

The Queen Victoria Maternity Hospital,
Rose Park,
South Australia.
November 18, 1960.

POLIOMYELITIS VACCINATION.

SIR: It is with regret, but with no surprise, that I note yet another encroachment on the medical profession's right to prescribe, and with many others wonder what the next encroachment will be. As from December 1 we will be under the control of local councils if we desire to use poliomyelitis vaccine.

This present interference should be opposed by all members, since to have to answer to a benevolent council as well as a benevolent Government is, without a doubt, the whole wedge and not just the thick end.

I ask members why, in the name of our dying professional freedom, we should: (i) collect our own vaccine or make ourselves known to some clerk or otherwise at the council chambers; (ii) be told how to keep vaccination records; (iii) submit written reports to the council "not later than the third day of the month to which the forms relate"; (iv) account to councils for all vaccine used or not used.

It is my opinion that there will be no end to this, but the least we could do is to refuse to give poliomyelitis vaccine except on prescription, and with complete freedom from forms, reports, councils and any other interference.

Yours, etc.,

J. F. GENDLE.

28 Woodward Avenue,
Strathfield,
N.S.W.
November 16, 1960.

HYPOGLYCÆMIC EFFECT OF CHLORPROPAMIDE.

SIR: We read with interest the case report on the hypoglycæmic effect of chlorpropamide (D. S. Pryor, MED. J. AUST., October 1, 1960), and would like to present a further case:

Mrs. G., aged 69, was admitted to the Queen Elizabeth Hospital on July 6, 1960, with a gangrenous big toe. She had been a known diabetic for 12 years; lately treated with chlorpropamide. She had symptoms of widespread arteriosclerosis; arteriosclerotic Parkinsonism, anginal pain and intermittent claudication. She had also had a number of "dizzy spells" over the previous few months.

She was given chlorpropamide, three and a half tablets (875 mg.) at 6 a.m. on July 7, 1960, as she said that this was her usual dosage. At 4 p.m. she lapsed into unconsciousness, after feeling hungry and irritable over the previous 30 minutes. She responded immediately to 30 ml. of 50% dextrose intravenously. She was again brought out of coma by 20 ml. of 50% dextrose at 9.15 p.m., and by a further 30 ml. at 12.45 a.m. A further 50 ml. were given for another comatose episode at 2.15 p.m. on July 8, 1960 (32 hours after chlorpropamide). She had been having small meals and glucose fluids throughout this period. To facilitate

management, a gastric tube was passed and 25% glucose fluids given for three days. Her urine did not show sugar until 86 hours after the chlorpropamide.

TABLE I.
Blood Sugar Estimations.

Date (1960).	Time.	Blood Sugar. (Mg. per 100 ml.)	Hours after Chlorpropamide.
July 7	4 p.m.	42	10
	9 p.m.	40	15
July 8	12.30 a.m.	39	18½
	9.30 a.m.	68	27½
	4.30 p.m.	102	34½
July 9	8.45 a.m.	75	50½
July 11	6 a.m.	460	96

Other investigations: blood examination normal; serum electrolytes normal; blood urea nitrogen 17 mg. per 100 ml.

It was subsequently ascertained from her referring doctor that her normal chlorpropamide dosage was two and a half tablets (625 mg.) *mane*.

She was stabilized on Semilente Insulin 16 units *mane*, 8 units *nocte*. She was submitted to surgery for her gangrene, but died some six weeks later.

Our experience confirms previous reports of the severity and prolonged duration of the hypoglycæmic effect of chlorpropamide. Permanent brain damage following chlorpropamide hypoglycæmia has been reported (Sackner and Balian[1]).

Our thanks are due to Dr. R. A. Burston, under whom this patient was admitted, for permission to publish the case.

Yours, etc.,

E. URBAN,
Medical Registrar;

T. ALDOR,
Resident Medical Officer.

The Queen Elizabeth Hospital,
Woodville,
South Australia.
October 24, 1960.

TYPISTS' ERRORS AND DOCTORS' HANDWRITING.

SIR: Dr. J. S. Barr-David's letter of November 5, 1960, reminded me of a triumphant banishment of a guilt-complex occasioned by a life-time of illegible handwriting.

After reading in the "Puffin Picture Book" "Better Handwriting" that "you can go on enjoying hand-writing until you are eighty", my mind was made up. Now I can read my own history notes and chemists can read my prescriptions!

The remedy lies in the Italic method, and with it one is in good company with Michael Angelo, Mary, Queen of Scots and her rival, Queen Elizabeth I.

Yours, etc.,

44 Domain Street,
South Yarra.
November 8, 1960.

CANCELLEROSCA CURSIVA.

ARTIFICIAL RESPIRATION FROM DROWNING.

SIR: Methods of artificial respiration for drowning wax and wane, but results will not improve until more attention is given to the water in the bronchi and bronchioles.

I would suggest that before any method of artificial respiration be started, the patient be held vertically with the head down and legs upwards. The tongue should then be pulled out with a clip and all the water allowed to drain out.

If possible, also, a medical practitioner should be in complete control of all manœuvres. I can remember witnessing unsuccessful attempts at resuscitation when I have been more controlled than in control.

Yours, etc.,

City Beach,
Western Australia.
November 9, 1960.

F. W. SIMPSON.

[1] *Amer. J. Med.*, 1960, 28: 135.

Medical Matters in Parliament.

HOUSE OF REPRESENTATIVES.

THE following extracts from *Hansard* relate to the proceedings of the House of Representatives.

October 27, 1960.

Therapeutic Substances Act.

MR. WHITLAM asked the Minister for Health, upon notice:

1. What additions and amendments have been made to the British Pharmaceutical Codex and the British Pharmacopœia since the *Therapeutic Substances Act* 1959?

2. When were they made?

3. Which of them have been gazetted under the Act?

4. When did they take effect for the purposes of the Act?

DR. DONALD CAMERON: The answers to the honourable member's questions are as follows:

1, 2, 3 and 4. No additions or amendments have been made to the British Pharmacopœia since the *Therapeutic Substances Act* 1959. A new edition of the British Pharmaceutical Codex became official in the United Kingdom in July, 1960. This has not yet been promulgated in Australia.

National Health Act.

MR. WHITLAM asked the Minister for Health, upon notice:

1. What additions or amendments have been made to the British Pharmacopœia since the *National Health Act* 1959?

2. When were they made?

3. Which of them have been gazetted under the Act?

4. When did they take effect for the purposes of the Act?

DR. DONALD CAMERON: The answers to the honourable member's questions are as follows:

1. None.

2, 3 and 4. See 1.

Drugs.

MR. WHITLAM asked the Minister for Health, upon notice:

1. Did he on 4th October, 1960, declare the drugs carbromal and bromvaletone to be poisons for the purposes of the Australian Capital Territory Poisons and Dangerous Drugs Ordinance?

2. Has the National Health and Medical Research Council recommended that these drugs should be declared to be poisons for the purposes of corresponding State legislation?

3. When did the Council make this recommendation?

4. When was the recommendation transmitted to the States?

5. Which States have made such declarations, and when did they do so?

DR. DONALD CAMERON: The answers to the honourable member's questions are as follows:

1. Yes.

2. Yes.

3. May, 1956.

4. June, 1956.

5. All States have declared these drugs as poisons and have so controlled them for a number of years.

Radioactive Substances.

MR. WHITLAM asked the Minister for Health, upon notice:

1. When did the National Health and Medical Research Council amend its model *Radioactive Substances Act* and regulations to require registration of X-ray equipment for use on humans?

2. When were the amendments transmitted to the States?

3. Which States have enacted and adopted the amendments and when did they come into operation?

DR. DONALD CAMERON: The answers to the honourable member's questions are as follows:

1. November, 1959.

2. March, 1960.

3. None.

Drugs.

MR. WHITLAM asked the Minister for Health, upon notice:

1. Which States have enacted the model act and adopted the model regulations which the National Health and Medical Research Council recommended in November, 1952, in relation to narcotic drugs?

2. When did the State acts and regulations come into operation?

DR. DONALD CAMERON: The answers to the honourable member's questions are as follows:

1 and 2. Legislation enacted in Queensland and South Australia relating to narcotic drugs is, for practical purposes, very similar to the model act and regulations recommended by the National Health and Medical Research Council. Tasmania brought in an act in 1959 which is based on the model act, but regulations have not yet been passed and the act is not yet in operation.

November 8, 1960.

Hospital Benefits.

MR. REYNOLDS: My question is addressed to the Minister for Health. In view of considerable public confusion regarding the operation of the special fund account covering hospital charges, will the Minister outline to the House the main provisions of this account?

DR. DONALD CAMERON: I must make a brief reply to the honourable member. The special account for hospitals, to which I think he is referring, ensures to patients who were previously refused fund benefit a means whereby they can obtain what amounts to fund benefit but what is known as special account benefit. The fund transfers the patient to the special account in certain circumstances, such as when the ailment in question is what is called a pre-existing ailment, or when the patient has attained the age of 65 years. The fund then pays the Commonwealth benefit plus the special account rate of benefit for the period the patient is in hospital in the case of a patient suffering from a pre-existing ailment, or, in the case of a patient transferred because of having reached the age of 65 years, the Commonwealth benefit, plus the rate of benefit for which the patient has insured himself with a benefit fund until he has exhausted what is called his maximum benefit period for the year, after which the rate falls to the special account rate for the remainder of his stay in hospital. There are a few other aspects of the matter that I could explain, but I thank that what I have said will be sufficient to answer the honourable member's question.

Repatriation Benefits.

MR. DUTHIE asked the Minister representing the Minister for Repatriation, upon notice:

How many ex-servicemen in each State who were in receipt of 10 per cent. and 15 per cent. pensions had their pensions cancelled during 1959 and 1960.

DR. DONALD CAMERON: I have been advised by the Minister for Repatriation as follows:

Ten per cent. and 15 per cent. member's pensions cancelled.

1958-1959—	Departmental Action.	Deceased.
New South Wales	54	165
Victoria	75	130
Queensland	45	45
South Australia	37	29
Western Australia	45	51
Tasmania	4	3
	260	423

1959-1960—	Departmental Action.	Deceased.
New South Wales	41	170
Victoria	76	96
Queensland	18	49
South Australia	56	33
Western Australia	46	51
Tasmania	1	3
	238	402

MR. CHANEY asked the Minister representing the Minister for Repatriation, upon notice:

What is the number of ex-servicemen under the age of 60 who are receiving a service pension in (*a*) Australia and (*b*) each State?

DR. DONALD CAMERON: I have been advised by the Minister for Repatriation that the answer to the honourable member's question is:

(*a*) As at 30th June, 1960, there were 2,089 ex-service personnel in Australia under the age of 60 in receipt of service pensions.

(*b*) These were divided by States, as follows:

New South Wales	646
Victoria	470
Queensland	412
South Australia	205
Western Australia	223
Tasmania	133
Total	2,089

Pensioner Medical Service.

MR. WHITLAM asked the Minister representing the Minister for Repatriation, upon notice:

When and how did the Repatriation Department advise totally and permanently incapacitated pensioners that their wives could be received into the Pensioner Medical Service between (*a*) the *Social Services Act* (No. 2), 1955 coming into operation on 19th October, 1955, and (*b*) December, 1953, means test being reimposed on 31st October, 1955?

DR. DONALD CAMERONS I have been advised by the Minister for Repatriation as follows:

The announcement that the conditions of eligibility into the Pensioner Medical Service would be varied on and after 31st October, 1955, was made on behalf of the Government on 7th October, 1955, by the Minister for Health, the Minister responsible for the administration of that service.

No action was taken by the Repatriation Department to specifically advise totally and permanently incapacitated members eligible for a service pension.

The Minister for Repatriation advises me that he did, however, by telegram to the various ex-service organizations sent on 20th October, 1955, advise them, that persons claiming eligibility for a service pension, should lodge their applications immediately.

MR. BEAZLEY asked the Minister for Social Services, upon notice:

1. How many aboriginal mothers were paid maternity allowances in the financial years 1957-58, 1958-59 and 1959-60 on the ground that they had been granted exemption under State law?

2. How many aboriginal mothers, though not granted exemption under State law, were granted maternity allowances during the same years on the ground of "character, standard of intelligence, and social development"?

3. How many aboriginal mothers during those years were refused maternity allowances on the grounds that they were not exempt from State law and did not qualify as to "character, standard of intelligence and social development"?

MR. ROBERTSON: The answers to the honourable member's questions are as follows:

1 and 2. Records have not been maintained of the number of aboriginal natives who have been granted maternity allowances.

3. Until February of this year maternity allowance was payable to an aboriginal mother only if—(*a*) she was for the time being exempt from the provisions of the law of the State or Territory in which she resided relating to the control of aboriginal natives; or (*b*) she resided in a State or Territory the law of which does not make provision for such exemption, and the Director-General of Social Services was satisfied that, by reason of the character and of the standard of intelligence and social development of the native, it was desirable that a maternity allowance should

be granted to her. The number of cases in which the claimants failed to satisfy qualification (a) are: 1957-58, 112; 1958-59, 77; July, 1959-February, 1960, 70. No claims were rejected because the claimants failed to satisfy qualification (b). Since February of this year, arising out of legislation introduced by this Government, all aboriginal mothers, except those who are nomadic or primitive, are entitled to maternity allowance.

November 10, 1960.

Aborigines.

MR. BEAZLEY asked the Minister for Territories, upon notice:

1. Were the aboriginal reserves of 69,458 square miles in the Northern Territory fortuitously selected from lands not wanted or taken up by Europeans or were they deliberately selected as terrain suitable for the aboriginal way of life?

2. Is there any instance of leased land being resumed from Europeans as an aboriginal reserve?

3. What steps have been taken in the reserves to foster the development of game for aboriginal hunting purposes and to provide other foodstuffs and water supplies?

4. What steps are taken to survey periodically the general health, nutrition and survival rate of aborigines on the reserves?

MR. HASLUCK: The answers to the honourable member's questions are as follows:

1. Some of the aboriginal reserves were selected because of their appropriateness as tribal lands for the aboriginal people whose special needs they were intended to meet. Such reservs include the Arnhem Land Reserve, Daly River and Haasts Bluff. Others have been selected more recently from unalienated Crown lands to meet the needs of particular aboriginal groups, e.g., Yuendumu Reserve and the recently declared South West Reserve.

2. Yes.

3. No steps have been taken to foster the development of game for aboriginal hunting purposes on the reserves. On the other hand, active steps have been taken to develop cattle herds and herds of other livestock to provide regular supplies of meat for the aboriginal population. Fodder crops have been grown and orchards and market gardens have been developed at all settlements and missions on reserves.

4. Most of the settlements and missions are on aboriginal reserves and a continuous check on the general health and nutrition of the aborigines on the reserves is maintained by the Commonwealth Department of Health and officers of the Welfare Branch of the Northern Territory Administration. A Medical Survey Officer visits settlements and missions on a five-weekly schedule. In addition to giving advice and indicating treatment in cases referred to him the medical officer periodically surveys the whole group for pathological conditions including trachoma, leprosy and tuberculosis. Infant weight cards are maintained by nursing sisters on settlements and missions in respect of infants and are checked regularly by medical officers during their survey visits. The Regional Dietitian attached to the Department of Health makes regular visits to settlements and missions and catering officers of the Welfare Branch of the Northern Territory Administration conduct regular inspections of settlements and missions and advise on the preparation of food for the native people and their families. Periodic visits are made by dentists to all settlements and missions. A mass T.B. survey was conducted by the Health Department in the Territory last year and the majority of natives on the reserves were examined. Hook-worm surveys are carried out from time to time and treatment is given whenever necessary.

MR. WARD asked the Prime Minister, upon notice:

1. How many aborigines were resident in Australia at the earliest date for which figures are available?

2. In what year did the number of resident aborigines reach its peak?

3. What is the present number according to the latest figures available?

MR. MENZIES: The answers to the honourable member's questions are as follows:

1 and 2. Dependable estimates of the number of aborigines in Australia are available only for very recent years. On page 328 of the Official Year Book No. 46, 1960, reference is made to earlier year books in which accounts were given of efforts to estimate the aboriginal population at the time of the first settlement.

3. The latest estimate by the Commonwealth Statistician is that there were 39,319 full-blood aborigines in Australia as at 30th June, 1954. At the census taken at the same date, 31,359 half-caste aborigines were recorded.

Infant Welfare in the Northern Territory.

MR. BEAZLEY asked the Minister for Territories, upon notice:

1. What is the infant mortality rate for (a) Europeans and (b) aborigines in the Northern Territory?

2. What is his department doing in relation to the pre-natal and post-natal care of aboriginal infants?

3. Does the department recognize any special difficulties in the survival of aboriginal infants as contrasted with Europeans; if so, what specific steps are being taken to ensure survival?

MR. HASLUCK: The answers to the honourable member's questions are as follows:

1. The infant mortality rate per 1000 live births for children under one year in the Northern Territory is:

Calendar Year.	Europeans.	Aborigines.
1957	34·06	117
1958	31·56	114
1959	38·93	102

The figures for Europeans have been extracted from the relevant Commonwealth "Year Books", while those for aborigines have been compiled by the Welfare Branch of the Northern Territory Administration, with the cooperation of the Registrar of Births, Deaths and Marriages. There was a net increase in the aboriginal population in the years 1957 to 1959 of between 1 and 2 per cent. per annum.

2. Infant welfare and nursing services have been established on twelve government settlements with a staff of twenty qualified nursing sisters and on all fourteen mission stations where eighteen qualified nursing sisters are employed. Under the direction of Commonwealth Department of Health medical officers and nurses a nursing aide is doing infant welfare work at the remaining small government settlement. One pastoral property employs a nursing sister for whom a government subsidy is paid and negotiations are in hand with two other pastoral managements for similar employment for nursing sisters. Medical officers of the Commonwealth Department of Health visit all settlements and missions and pastoral properties with air-strips on a five-weekly schedule. Irregular visits are made by road to other pastoral properties. Visits are made by Department of Health nursing sisters approximately twice a year.

3. The problems of personal hygiene leading to infection with dysentery in its various forms, malnutrition due in large part to ignorance and primitive habits and neglected bronchial complaints leading to pneumonia, are major contributors to the high infant mortality rate. In addition, some aboriginal parents are not themselves as keenly aware as European parents of the services available and the value of them to children. By gradually improving the personal health and hygiene standards of parents and children, by improved pre-natal and post-natal care and feeding of mothers, by improved infant feeding, by training older school-girls in infant care, by improvement of household facilities, and by training of natives in more effective use of houses, latrines and ablution and laundry facilities, it is expected that the incidence of deaths in this infant group will be progressively reduced.

SENATE.

THE following extracts from *Hansard* relate to the proceedings of the Senate.

October 19, 1960.

Repatriation General Hospital, Springbank.

SENATOR LAUGHT: Can the Minister for Repatriation state whether he has approved any plans to improve the accommodation for the treatment of psychiatric cases at the Repatriation General Hospital in Daws Road, Springbank, Adelaide? If he has, what plans has he approved? Is there anything that he can do to implement such plans? Does

the fact that legislation widening the scope of repatriation treatment has been passed recently make the need for increased hospital accommodation more urgent than ever before?

SENATOR SIR WALTER COOPER: For some years many representations have been made by South Australian parliamentary representatives that the psychiatric wards at the Springbank Hospital should be demolished and up-to-date wards should be built. The wards mentioned by the honourable senator were built during war-time. We do not say that they are up to the standard at which we aim at the present time. Over the last three or four years plans have been made for demolishing those buildings and erecting new wards. It was hoped that we would be able to start on the new buildings this year. Plans were prepared and passed, and we were ready to go ahead; but unfortunately the money was not available for the work this year. We had a big contract for the rebuilding of wards at the Hobart Hospital. Those wards were erected as temporary wards during the 1914-1918 war. The provision for that work at the Hobart Hospital in this year's estimate for the Repatriation Department is about £260,000 of the total estimate of £427,000 for the department. In order to go ahead with the plans for Springbank we would have to drop the Hobart project. Personally, I think the Hobart wards were in a much worse condition than the Springbank wards. So we have gone ahead with the work in Hobart. That does not mean that the Springbank project will be dropped. We will go ahead with that job as early as we possibly can. I am looking forward to the Springbank Hospital having up-to-date psychiatric wards and I have no doubt that it will have such wards.

The legislation that has recently been passed — giving service pensioners full rights under regulation 66 of the regulations under the *Repatriation Act* to treatment for non-war caused disabilities, including hospital accommodation and medicines—will make no difference to the accommodation provided in the psychiatric wards at the Springbank Hospital. There is accommodation for those service pensioners in the general wards at Springbank. The South Australian service pensioners will have that accommodation available to them. There will be no difficulty in providing for their requirements at the Springbank Hospital.

Pharmaceutical Benefits.

SENATOR PEARSON asked the Minister representing the Minister for Health, upon notice:

Is it a fact that repeats of a prescription for a medicine on the free list, prescribed by a doctor under the Commonwealth Government's health scheme, carry a charge of 5s. per repeat, when authorized by the doctor on the original prescription?

SENATOR HENTY: The Minister for Health has now furnished the following reply:

No charge is made for the supply of pharmaceutical benefits to pensioners and their dependants who are in possession of a Pensioner Medical Service entitlement card. A charge of 5s. is payable for the supply of a pharmaceutical benefit to other persons and this charge is also payable for each repeat.

Hearing Aids.

SENATOR TANGNEY asked the Minister representing the Minister for Health and Minister in charge of the Commonwealth Scientific and Industrial Research Organization, upon notice:

1. Is it a fact that the manufacture by the Commonwealth Serum Laboratories of Salk vaccines and antibiotics has guaranteed that they are available to the public at a very low cost, in which the profit factor is not a consideration?

2. If so, in view of the high cost to the public of hearing aids, etc., will the Minister give consideration to research by the Commonwealth Scientific and Industrial Research Organization into the various types of hearing aids with a view to their production so that only the very best will be available to the public without exploitation of their misfortune?

SENATOR HENTY: The Minister for Health has now furnished the following reply:

1. Salk vaccine is manufactured by the Commonwealth Serum Laboratories and is available to the public without charge. Penicillin is manufactured by the Commonwealth Serum Laboratories and is available as a pharmaceutical benefit under the *National Health Act*. The Commonwealth Serum Laboratories were established for public health reasons and are not conducted for the profit of individuals.

2. The Commonwealth Acoustic Laboratories provide first-class hearing aids free of charge to children and various other special groups in the community requiring assistance, including ex-servicemen eligible for this service under the *Repatriation Act*.

Broad Spectrum Antibiotics.

SENATOR PEARSON asked the Minister representing the Minister for Health, upon notice:

As pharmaceutical benefits absorb 50 per cent. of the national health scheme expenditure and approximately 58 per cent. of this is spent on "broad spectrums", will the Minister investigate the possibility of more broad spectrum antibiotics being manufactured by the Commonwealth Serum Laboratories, thus avoiding the expenses of importing them and so effecting a saving in the cost of the national health scheme?

SENATOR HENTY: The Minister for Health has now furnished the following reply:

Yes.

October 25, 1960.

Drugs.

SENATOR MCMANUS: I direct three questions to the Minister for Customs and Excise. Is it a fact that, because of the operations of the United Nations agency set up for the purpose of suppressing the drug traffic, the illegal importation into America and Europe of dangerous narcotic drugs from the East has been significantly decreased? Is it also a fact that, as a result, those concerned in this nefarious smuggling traffic have decided to turn their attention to Australia as a potential market, particularly for heroin? If so, has the Government undertaken, or has it in mind to undertake, a strengthening of our customs and other barriers against the importation of dangerous narcotics?

SENATOR HENTY: I understand that the importation of narcotics to the United States of America and Europe has been reduced as a result of the work of customs and other officers in those areas. My department is in touch with corresponding departments in other countries. We are kept constantly advised of all the latest methods of detection and of means of trying to introduce dangerous drugs into various countries. We are aware that, as the markets of Europe and America are denied to people engaged in this trade, they may attempt to introduce narcotics into Australia. We are fully alive to that possibility. We are watching the position most carefully and we shall do everything possible to see that these people are not successful.

October 26, 1960.

Tuberculosis.

SENATOR ROBERTSON asked the Minister representing the Minister for Health, upon notice:

1. Is it a fact, as stated in the Press, that tuberculosis is very prevalent in our midst, especially among migrants?

2. Is anti-tuberculosis work made possible by the financial assistance of the Commonwealth Government to patients and their dependants, making Australia practically free of this killer disease?

3. Has the success in this field led to the closing down of many sanatoria?

4. If the Press statement is true that one migrant in 883 examined has had active tuberculosis, does this not indicate the need for stricter medical examination at ports of embarkation?

SENATOR HENTY: The Minister for Health has now furnished the following reply:

1. No. Tuberculosis cannot be regarded as very prevalent in this country among those born either in or outside Australia. The rate of newly notified cases in Australia is one of the lowest in the world. There has been an increase of new notifications this year in New South Wales and Victoria, but this is due to more active case finding and not to any real increase in the prevalence of the disease.

2. No. Australia cannot be considered to be practically free of this killer disease, as during the financial year which ended on 30th June, 1960, 3983 persons were newly notified as suffering from tuberculosis. However, as a result of the provisions at Commonwealth expense of adequate facilities for diagnosis and treatment, and as a result of the use of modern anti-tuberculosis drugs, the death rate has been reduced from 28·1 per 100,000 in 1948 to just over 5 per 100,000. Nevertheless, if further progress is to be achieved, our efforts to control the disease, on which the Commonwealth has spent over £65 million, cannot be relaxed.

3. Yes, some sanatoria have been diverted to uses other than for tuberculosis patients, as there are fewer persons in need of treatment than when these institutions were planned, and modern drug treatment has greatly reduced the average duration of patients' stay in sanatoria.

4. The Press statement referred to relates to a special X-ray survey in New South Wales during 1959-1960, as a result of which 27 active cases were discovered in 23,861 migrants X-rayed (1 in 833) as compared with 50 active cases among 76,103 persons born in Australia (1 in 1511). However, out of a total of 422,002 persons X-rayed during the same year in New South Wales, in a more comprehensive mass survey, only 77 of the 258 active cases discovered were migrants. It is interesting to note that of these 77 migrants, three had arrived in Australia before 1900, one as early as 1880, 37 before 1940, i.e. before World War II, and of the 40 who arrived since the end of this war, only 28 within the last ten years, i.e. an average of 2·8 migrants per year examined. It should also be noted that non-assisted British migrants are not required to have a chest radiograph before their departure from the United Kingdom. All assisted migrants and all non-British persons who pay their own fares are obliged to have a medical examination, which includes a chest radiograph, before acceptance for an assisted passage or visé. The examinations are very thorough and any person with active or doubtfully active tuberculosis is rejected.

Royal Australasian College of Surgeons.

FINAL FELLOWSHIP EXAMINATION.

A MEETING of the Court of Examiners for the final examination for fellowship of the Royal Australasian College of Surgeons will be held in Sydney, commencing on or about Friday, May 12, 1961. Candidates who desire to present themselves at this examination should apply on the prescribed form to the Censor-in-Chief for permission to do so before March 30, 1961. The appropriate forms are available from the Examination Secretary, Royal Australasian College of Surgeons, Spring Street, Melbourne, C.1. Candidates who have already been approved by the Censor-in-Chief, but who have not yet presented themselves for the examination, may present for this examination, provided they notify the Examination Secretary of their intention to do so by March 30, 1961. It is stressed that entries will close on this day and late entries cannot be accepted. The examination fee is £31 10s. plus exchange on cheques drawn on banks outside Melbourne, and must be paid to the Examination Secretary by March 30, 1961. The examination will be conducted in general surgery and in the special branches of ophthalmology, laryngo-otology, orthopædics, gynæcology and operative obstetrics, urology, thoracic surgery, neurosurgery, plastic surgery and pædiatric surgery.

At its meeting held on June 20, 1958, the Council of the College decided that candidates who possessed the fellowship of a body with which this College has reciprocity of primary examinations shall be exempted from the written part of the final examination, provided that there is no relaxation of apprenticeship prerequisites.

FACULTY OF ANÆSTHETISTS.

Final Fellowship Examination.

A MEETING of the Court of Examiners for the final examination for fellowship of the Faculty of Anæsthetists of the Royal Australasian College of Surgeons will be held in Sydney, commencing on or about Friday, May 12, 1961. Candidates who desire to present themselves at this examination should apply on the prescribed form to the Assessor for permission to do so before March 30, 1961. The appropriate forms are available from the Examination Secretary of the Faculty, Royal Australasian College of Surgeons, Spring Street, Melbourne, C.1. Candidates who have already been approved by the Assessor, but who have not presented themselves for the examination, may present for this examination, provided that they notify the Examination Secretary of their intention to do so by March 30, 1961. It is stressed that entries close on this day and late entries cannot be accepted. The examination fee is £31 10s., plus exchange on cheques drawn on banks outside Melbourne, and must be paid to the Examination Secretary by March 30, 1961. Subjects for the final examination are: (*a*) anæsthesia and analgesia, including pre-operative and post-operative care; (*b*) medicine and surgery; (*c*) the application of the basic sciences, including chemistry and physics, to the specialty of anæsthetics. The examination in each case is partly written, partly oral and partly clinical (including the examination of patients).

Candidates are advised that the primary examination for fellowship of the Faculty of Anæsthetists, Royal College of Surgeons of England, is reciprocal with the primary examination of this Faculty. Graduates of an approved medical school who have obtained, prior to December 31, 1957, the first part of the diploma in anæsthesia of an approved medical school or college, may, at the discretion of the Board, be allowed to present for the final examination for fellowship of the Faculty, provided they have fulfilled all other regulations. In addition, a Board of Censors type examination will be held at the same time, and those eligible are: (i) foundation members of the Faculty of Anæsthetists of the Royal Australasian College of Surgeons, who were graduates of at least 25 years on January 1, 1960; (ii) members of the Faculty of Anæsthetists of the Royal Australasian College of Surgeons who hold a two-part diploma in anæsthesia or the fellowship of the Faculty of Anæsthetists of the Royal College of Surgeons of England; (iii) Fellows of the Faculty of Anæsthetists of the Royal College of Surgeons of England who possessed their Fellowship prior to January 1, 1960. The conditions as outlined above in regard to the manner of entry and the examination fee also apply to the Board of Censors type examination.

World Medical Association.

FOURTEENTH GENERAL ASSEMBLY.

AMONGST matters covered by resolutions adopted at the Fourteenth General Assembly of the World Medical Association held in Berlin in September, 1960, were the following:

Reaffirmation of W.M.A. Objectives.

The Fourteenth General Assembly declared again the importance of the objectives of the World Medical Association to the medical profession throughout the world and to all mankind. The General Assembly requested that the Council and its staff use all available means to increase the support of W.M.A. not only from present member associations but also from among other national associations that are not now members.

Aid in Catastrophe.

The Fourteenth General Assembly directed Counci. to establish a programme for emergency care and explore the possibility of coordinating the programme with those of the International Red Cross and other groups offering similar services.

Aid to Aging Population.

The General Assembly went on record as approving and wishing to encourage the efforts of the national medical associations and other organizations in providing adequate medical care and solving the socio-economic problems associated with the increase of the aged in the population in conformity with the national needs and the recognized social system of each country.

Commendation of Peruvian Medical Federation.

The W.M.A. paid tribute to the Peruvian Medical Federation for its continued defence of the Twelve Principles of Medical Care under Social Security. It encouraged and pledged its support to the Peruvian doctors in continuing to insist that these principles be observed and govern medical service under the social security system.

Creation of African Region.

The Fourteenth General Assembly approved the creation of an African Region within its regional structure. Council directed that a survey of the member associations that are affected by this change in regional structure be carried out in order to determine the most effective and efficient way in which the directive contained in this resolution may be achieved.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes, etc., are published in the *Commonwealth of Australia Gazette*, No. 73, of October 27, 1960.

NAVAL FORCES OF THE COMMONWEALTH.

Permanent Naval Forces of the Commonwealth (Sea-Going Forces).

Appointments.—Elie Robert Emmanuel is appointed Surgeon Lieutenant (for Short Service) (on probation), dated 26th May, 1960.

Termination of Appointments.—The appointment of Ian Ivor Maynard MacGregor as Surgeon Lieutenant (for Short Service) is terminated, dated 8th July, 1960.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Reserve.

Appointments.—Harold Lindsay Thompson is appointed Surgeon Lieutenant with seniority in rank of 20th February, 1956, dated 20th February, 1960. Edmund Noel O'Brien is appointed Surgeon Lieutenant, dated 17th May, 1960.

Promotions.—Surgeon Lieutenants Geoffrey David Davis and George Robert Faithfull are promoted to the rank of Surgeon Lieutenant-Commander, dated 22nd April, 1960, and 28th May, 1960, respectively.

Ante-dating Seniority.—The seniority of Surgeon Lieutenant Kenneth Aubrey Boulton is ante-dated to 28th December, 1956, dated 18th March, 1960.

Termination of Appointment.—The appointment of John Bedlington Jolley as Surgeon Lieutenant is terminated, dated 27th June, 1960.

AUSTRALIAN MILITARY FORCES.

Australian Regular Army.

Royal Australian Army Medical Corps (Medical).

3/37652 Major-General W. D. Refshauge, C.B.E., relinquishes the appointment of Director-General of Medical Services, 31st August, 1960, and is transferred to the Citizen Military Forces, Unattached List (Royal Australian Army Medical Corps (Medical)), Southern Command, 1st September, 1960.

Northern Command.

Royal Australian Army Medical Corps (Medical).—1/39204 Captain H. R. Withers is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)), (Northern Command), 10th August, 1960.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—The following officers are transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Eastern Command):—Captains 5/26587 R. L. Bissett, 18th July, 1960, and 2/134210 V. J. Adcock, 21st July, 1960. The provisional appointment of 2/130131 Captain G. B. Field is terminated, 28th October, 1959.

Southern Command.

Royal Australian Army Medical Corps (Medical).—The notification respecting 3/82441 Lieutenant-Colonel D. C. Cowling which appeared in Executive Minute No. 45 of 1960, promulgated in Commonwealth Gazette No. 48 of 1960, is withdrawn. 3/159739 Major (Honorary Lieutenant-Colonel) R. A. Philip is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Southern Command), 10th June, 1960. 3/50087 Lieutenant-Colonel H. J. B. Stephens is placed upon the Retired List (Southern Command) and is granted the military title of Lieutenant-Colonel with permission to wear the prescribed uniform, 15th August, 1960.

Central Command.

Royal Australian Army Medical Corps (Medical).—The provisional appointment of 4/38071 Captain H. T. W. Harris is terminated 25th August, 1960. *To be Captain (provisionally), 26th August, 1960*—4/38071 Henry Thomas Wilfred Harris.

Northern Territory Command.

Royal Australian Army Medical Corps (Medical).—The provisional appointment of 7/3015 Captain (Temporary Major) R. C. Webb is terminated, 8th April, 1960. *To be Captain (provisionally) (Temporary Major), 9th April, 1960*—7/3015 Ronald Campbell Webb.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps (Medical).

Northern Command.—The resignation of Honorary Captain R. H. Coates of his commission is accepted, 4th August, 1960.

Eastern Command.—Honorary Captain B. M. Allen is placed upon the Retired List (Eastern Command) and is granted the military title of Honorary Captain with permission to wear the prescribed uniform, 25th June, 1960.

Southern Command.—Honorary Captain J. P. Asche is retired, 17th August, 1960.

Western Command.—Honorary Captain L. D. Hodby is retired, 31st October, 1960.

The following officer is placed upon the Retired List and is granted military titles equivalent to the substantive or honorary rank shown, with permission to wear the prescribed uniform, 31st October, 1960.

Eastern Command.—Major C. H. Horsley.

The Royal College of Obstetricians and Gynaecologists.

REGIONAL COUNCIL IN AUSTRALIA.

Fotheringham Research Fellow.

THE Australian Regional Council of the Royal College of Obstetricians and Gynæcologists announces that the Fotheringham Research Fellow for 1960-1961 is Dr. W. H. Patterson, M.R.C.O.G., of New South Wales. Dr. Patterson's project is as follows:

> To study the vaginal smear during the pregnant and non-pregnant state and to evaluate its diagnostic and prognostic usefulness in conditions unassociated with pelvic malignant disease.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following additions and amendments have been made to the Register of Medical Practitioners for New South Wales, in accordance with the provisions of the *Medical Practitioners' Act*, 1938 (as amended).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (*a*) of the Act: Brown, David Dorey, M.B., Ch.B., 1916 (Univ. Melbourne); Buckmaster, Neil Stanley, M.B., B.S., 1952 (Univ. Melbourne), F.R.C.S. (England), 1959; Nicholls, Rosemary, M.B., B.S., 1955 (Univ. Melbourne).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (*b*) of the Act: Blake, Douglas Whitaker, M.B., Ch.B., 1955 (Univ. Glasgow); Dunlop, Ronald Yorston, M.B., Ch.B., 1933 (Univ. St. Andrews), D.T.M. (Liverpool), 1935, D.T.H. (Liverpool), 1935, D.P.H. (London), 1938, M.D., 1941 (Univ. St. Andrews); Fairbairn, George Gardyne, M.B., B.Ch., 1950 (Univ. Witwatersrand); Fergus, Basil Eric Talbot, M.B., Ch.B., 1950 (Univ. Capetown); Jose, Anthony Douglas, B.M., B.Ch., 1954 (Univ. Oxford), M.R.C.P. (London), 1957; Lotzof, Leonard, M.B., B.Ch., 1943 (Univ. Witwatersrand); Norman, Hugh McCormick, M.B., B.Ch., 1954 (Univ. Dublin); Rice, Douglas Gordon, M.B., B.Ch., 1950 (Q. University Belfast); Tulip, Ellen Mary, M.B., B.S., 1955 (Univ. Hong Kong).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (a) of the Act: Bricknell, Daniel, M.B., B.S., 1957 (Univ. Queensland); McCafferty, John Francis, M.B.,

Ch.B., 1958 (Univ. New Zealand); Muirden, John Colin, M.B., B.S., 1957 (Univ. Melbourne); Sims, Peter Barrington, M.B., B.S., 1958 (Univ. Melbourne); Stam, Robert Edward, M.B., B.S., 1949 (Univ. Adelaide), F.R.C.S. (Edinburgh), 1957; York, John Robert, M.B., B.S., 1957 (Univ. Melbourne).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (2A) of the Act: Halmagyi, Alice Julia, M.D., 1947 (Univ. Szeged); Kardos, Ida Magdalena, M.D., 1927 (Univ. Pecs); Stiggelbout, Willem, M.D., 1954 (Univ. Amsterdam), L.A.H. (Dublin), 1959, D.T.M. & H., R.C.P. & S. (England), 1957.

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1) (b) of the Act: Gregory, Patrick John, M.R.C.S. (England), L.R.C.P. (London), 1955, D.A., R.C.P. & S. (England), 1959; Hodgson, Harry James, M.B., B.Chir., 1956 (Univ. Cambridge); Jones, Alan Trengove, M.B., Ch.B., 1952 (Univ. Capetown); Smurthwaite, William Aston, M.R.C.S. (England), L.R.C.P. (London), 1942; White, James Alison, M.B., Ch.B., 1957 (Univ. Glasgow).

Registered medical practitioner who has complied with the requirements of Section 17 (3) and is registered under Section 17 (2A) of the Act; Malinowski, Henryk Leonard, M.D., 1936 (Univ. Bologna).

The following have been issued with interim licences under Section 21C(3) of the Act: Tziniolis, John Antony, Liverpool District Hospital; Majewski, Stanislaus, advice received of his resignation from Cessnock District Hospital, Licence is now inoperative, as from September 2, 1960.

The following has been issued with a licence under Section 21C (4) of the Act: Harasymczuk, Isjaslaw Leonid Plato, for one year, from September 5, 1960.

The following has been issued with a licence under Section 21C (3): Kainer, Yaaqov, for one year, from September 7, 1960.

The following has been issued with a licence under Section 21C (3): Kiss, Sarah, one year from October 10, 1960.

The following have been issued with a licence under Section 21A of the Act: Gerlach, Helmut, one year from December 1, 1960; Vall, Laszlo, one year from November 21, 1960.

The following have been issued with a licence under Section 21C (4) of the Act: Peukert, Joseph, one year from October 20, 1960; Malesevic, Bosko, one year from November 1, 1960; Miller, Halina, one year from October 6, 1960; Tziniolis, John Antony, one year from October 6, 1960; Wilcox, Eva, one year from November 4, 1960; Banathy, Laszlo Julius Joseph, one year from October 6, 1960; Staszkiw, Wladimir, one year from October 31, 1960; Ropicki, Lydia, one year from October 12, 1960; Siroky, Nandor Ferdinand, one year from November 26, 1960.

Post-Graduate Work.

THE BRITISH COUNCIL.

Course in Anæsthesia, London and Oxford.

A COURSE in anæsthesia will be held in London and Oxford from February 19 to March 4, 1961, under the auspices of the British Council in collaboration with the Faculty of Anæsthetists of the Royal College of Surgeons of England. Such a course has proved to be of the greatest interest to specialists in anæsthesia overseas, and the programme will follow the lines of previously successful courses. Many of the leading teaching and specialist hospitals will be visited, in some of which it will be possible to attend practical demonstrations in the operating theatres. The demonstrations will give members an opportunity of seeing the use of modern methods of anæsthesia in both diagnostic and therapeutic applications. It will therefore be possible to study the use of anæsthetic methods in a wide range of surgical applications.

To supplement the practical demonstrations there will be a series of lectures at the Royal College of Surgeons describing modern development in anæsthesia. Besides attending demonstrations and lectures, members will be able

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED OCTOBER 29, 1960.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	1	..	7(6)	..	..	..	..	..	c 8
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	5	..	5
Anthrax	..	1(1)	..	..	..	..	..	..	1
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	7(2)	16(15)	2(1)	..	..	..	1	..	26
Diphtheria	..	..	1	..	..	..	..	..	1
Dysentery (Bacillary)	..	2	..	..	1	..	..	..	3
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	1	..	..	..	..	..	..	1
Infective Hepatitis	159(94)	78(48)	22(6)	68(40)	8(4)	1(1)	2	3	341
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	2	..	2
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	2(1)	3(2)	..	..	..	..	..	..	5
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	2	..	..	..	3(2)	..	..	5
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	16(9)	1(1)	3(2)	5(4)	..	..	..	25
Salmonella Infection	..	..	..	5(3)	..	..	..	..	5
Scarlet Fever	4(4)	15(9)	7(3)	13(5)	..	1(1)	..	..	40
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	1	..	..	..	..	..	1
Trachoma	..	..	..	..	5(2)	..	..	..	5
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	34(21)	23(13)	24(11)	9(4)	7(5)	4(1)	..	..	101
Typhoid Fever	..	..	..	..	1(1)	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

to take part in informal discussions, based on the work observed in the hospitals, with those responsible for the practical and theoretical instruction on the course.

Applicants should be anæsthetists from overseas who have been wholly engaged in the specialty of anæsthetics for not less than two years, or surgeons interested in the way in which advanced techniques in anæsthesia can help them in their work. Not more than 20 members can be admitted to the course. Members will live in hotels in central London. The fee is £47. Applications should be made to the Representative, The British Council, 18 Greenoaks Avenue, Edgecliff, N.S.W.

Notes and News.

Venereal Disease Symposium.

Physicians and workers in allied fields who are interested in the venereal diseases are invited to participate in the Twelfth Annual Venereal Disease Symposium at the Hotel New Yorker in New York City on April 13 and 14, 1961. The Programme Committee for the 1961 symposium points out that reported cases of primary and secondary syphilis have increased 52% over the past year. The symposium is sponsored jointly by the American Venereal Disease Association and the Public Health Service. Information relating to the symposium may be obtained from Dr. William J. Brown, Program Committee Chairman, Venereal Disease Branch, Communicable Disease Center, Atlanta 22, Georgia, U.S.A.

Director of Student Health Service, University of Sydney.

Dr. T. D. Wilkins has been appointed Director of Student Health Service in the University of Sydney. A graduate of the University of Sydney, Dr. Wilkins has for the past ten years been engaged in general practice.

Medical Appointments.

THE following have been appointed Senior Resident Medical Officers at The Queen Elizabeth Hospital, Adelaide: Dr. M. W. Maddern, Dr. P. H. M. Barnes, Dr. J. I. Manson, Dr. B. W. Orchard, Dr. T. A. M. Aldor, Dr. C. Heaysman, Dr. J. S. H. Tooth.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Csillag, John, M.D., 1923 (Univ. Budapest), Reg. Section 21A, Ungarie Region, Ungarie.

Rush, Bryan McKay, M.B., B.S., 1957 (Univ. Sydney), 41 Springdale Road, Killara.

Roberts, Harley Stuart, M.B., B.S., 1959 (Univ. Sydney), 691 Mowbray Road, Chatswood.

Deaths.

THE following deaths have been announced.

LORGER.—Albert Eric Lorger, on September 9, 1960, at Parkes, N.S.W.

JOHNSON.—Vincent Phillip Johnson, on September 25, 1960, at Melbourne.

MCADAM.—Cecil Gordon McAdam, on November 16, 1960, at Melbourne.

SIMPSON.—George, on November 23, 1960, at Melbourne.

Diary for the Month.

DECEMBER 6.—New South Wales Branch, B.M.A.: Public Relations Committee. Organization and Science Committee 8 p.m. (with Special Groups 8.30 p.m.).

DECEMBER 7.—Victorian Branch, B.M.A.: Branch Meeting.

DECEMBER 7.—Victorian Branch, B.M.A.: Branch Council Meeting.

DECEMBER 7.—Western Australian Branch, B.M.A.: Branch Council Meeting.

DECEMBER 8.—New South Wales Branch, B.M.A.: Branch Meeting.

DECEMBER 9.—Tasmanian Branch, B.M.A.: Branch Council.

DECEMBER 9.—Queensland Branch, B.M.A.: Branch Council Meeting.

DECEMBER 12.—Victorian Branch, B.M.A.: Executive Meeting of Branch Council.

DECEMBER 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee. Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in Australia can become subscribers to the Journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £6 *per annum* within Australia and the British Commonwealth of Nations, and £7 10s. *per annum* within America and foreign countries, payable in advance.